

## TITLE OF THE INVENTION

### O-SUPERFAMILY CONOTOXIN PEPTIDES

## CROSS-REFERENCE TO RELATED APPLICATIONS

5 The present application is related to U.S. provisional patent applications Serial No. 60/173,754 filed 30 December 1999, Serial No. 60/214,263 filed 26 June 2000, Serial No. 60/219,440 filed 20 July 2000 and Serial No. 60/243,412 filed 27 October 2000.

10 This invention was made with Government support under Grant No. PO1 GM48677 awarded by the National Institute of General Medical Sciences, National Institutes of Health, Bethesda, Maryland. The United States Government has certain rights in the invention.

## BACKGROUND OF THE INVENTION

15 The invention relates to relatively short peptides (termed O-Superfamily conotoxins herein), about 20-40 residues in length, which are naturally available in minute amounts in the venom of the cone snails or analogous to the naturally available peptides, and which preferably include three disulfide bonds.

20 The publications and other materials used herein to illuminate the background of the invention, and in particular, cases to provide additional details respecting the practice, are incorporated by reference, and for convenience are referenced in the following text by author and date and are listed alphabetically by author in the appended bibliography.

25 *Conus* is a genus of predatory marine gastropods (snails) which envenomate their prey. Venomous cone snails use a highly developed apparatus to deliver their cocktail of toxic conotoxins into their prey. In fish-eating species such as *Conus magus* the cone detects the presence of the fish using chemosensors in its siphon. When close enough the cone extends its proboscis and impales the fish with a hollow harpoon-like tooth containing venom. This immobilizes the fish and enables the cone snail to wind it into its mouth via the tooth held at the end of its proboscis. For general information on *Conus* and their venom see the website address <http://grimwade.biochem.unimelb.edu.au/cone/referenc.html>. Prey capture is accomplished through a sophisticated arsenal of peptides which target specific ion channel and receptor subtypes. Each *Conus* species venom appears to contain a unique set of 50-200 peptides. The composition of the venom differs greatly between species and between individual snails within each species, each optimally evolved to paralyse its prey. The active components of the venom are small peptides

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toxins, typically 10-30 amino acid residues in length and are typically highly constrained peptides due to their high density of disulphide bonds.

The venoms consist of a large number of different peptide components that when separated exhibit a range of biological activities: when injected into mice they elicit a range of physiological responses from shaking to depression. The paralytic components of the venom that have been the focus of recent investigation are the  $\alpha$ -,  $\omega$ - and  $\mu$ -conotoxins. All of these conotoxins act by preventing neuronal communication, but each targets a different aspect of the process to achieve this. The  $\alpha$ -conotoxins target nicotinic ligand gated channels, the  $\mu$ -conotoxins target the voltage-gated sodium channels and the  $\omega$ -conotoxins target the voltage-gated calcium channels (Olivera et al., 1985; Olivera et al., 1990). For example a linkage has been established between  $\alpha$ -,  $\alpha$ A- &  $\psi$ -conotoxins and the nicotinic ligand-gated ion channel;  $\omega$ -conotoxins and the voltage-gated calcium channel;  $\mu$ -conotoxins and the voltage-gated sodium channel;  $\delta$ -conotoxins and the voltage-gated sodium channel;  $\kappa$ -conotoxins and the voltage-gated potassium channel; conantokins and the ligand-gated glutamate (NMDA) channel. Five  $\delta$ -conotoxins have been described: GmVIA (U.S. Patent No. 5,719,264); PVIA (U.S. Patent No. 5,739,276); TxVIA (Hillyard et al., 1989; Fainzilber et al., 1991); TxVIB (Fainzilber et al., 1991); NgVIA (Fainzilber et al., 1995); and TxIIA (Nakamura et al., 1996). For a partial list of *Conus* peptides and their amino acid sequences see the website address <http://pir.georgetown.edu>.

However, the structure and function of only a small minority of these peptides have been determined to date. For peptides where function has been determined, three classes of targets have been elucidated: voltage-gated ion channels; ligand-gated ion channels, and G-protein-linked receptors.

*Conus* peptides which target voltage-gated ion channels include those that delay the inactivation of sodium channels, as well as blockers specific for sodium channels, calcium channels and potassium channels. Peptides that target ligand-gated ion channels include antagonists of NMDA and serotonin receptors, as well as competitive and noncompetitive nicotinic receptor antagonists. Peptides which act on G-protein receptors include neurotensin and vasopressin receptor agonists. The unprecedented pharmaceutical selectivity of conotoxins is at least in part defined by a specific disulfide bond frameworks combined with hypervariable amino acids within disulfide loops (for a review see McIntosh et al., 1998).

Potassium channels comprise a large and diverse group of proteins that, through maintenance of the cellular membrane potential, are fundamental in normal biological function.

These channels are vital in controlling the resting membrane potential in excitable cells and can be broadly sub-divided into three classes: voltage-gated K<sup>+</sup> channels, Ca<sup>2+</sup> activated K<sup>+</sup> channels and ATP-sensitive K<sup>+</sup> channels. Many disorders are associated with abnormal flow of potassium ions through these channels. The identification of agents which would regulate the flow of potassium ions through each of these channel types would be useful in treating disorders associated with such abnormal flow.

It is desired to identify additional conotoxin peptides having activities of the above conopeptides, as well as conotoxin peptides having additional activities.

## 10 SUMMARY OF THE INVENTION

The invention relates to relatively short peptides (termed O-Superfamily conotoxins herein), about 20-40 residues in length, which are naturally available in minute amounts in the venom of the cone snails or analogous to the naturally available peptides, and which preferably include three disulfide bonds. The O-superfamily conotoxins include  $\omega$ -conotoxins,  $\kappa$ -conotoxins,  $\delta$ -conotoxins,  $\mu$ O-conotoxins and GS conotoxin.

Thus, in one embodiment, the present invention is directed to the conotoxin peptides set forth in Table 2 and the corresponding peptides set forth in Table 1.

In a second embodiment, the present invention is directed to all of the propeptides and nucleic acid sequences encoding the propeptides or peptides set forth in Table 1.

In a third embodiment, the present invention is directed to derivatives or pharmaceutically acceptable salts of the conotoxin peptides disclosed herein. Examples of derivatives include peptides in which the Arg residues may be substituted by Lys, ornithine, homoargine, nor-Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any synthetic basic amino acid; the Lys residues may be substituted by Arg, ornithine, homoargine, nor-Lys, or any synthetic basic amino acid; the Tyr residues may be substituted with <sup>125</sup>I-Tyr, meta-Tyr, ortho-Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any synthetic hydroxy containing amino acid; the Ser residues may be substituted with Thr or any synthetic hydroxylated amino acid; the Thr residues may be substituted with Ser or any synthetic hydroxylated amino acid; the Phe residues may be substituted with any synthetic aromatic amino acid; the Trp residues may be substituted with Trp (D), neo-Trp, halo-Trp (D or L) or any aromatic synthetic amino acid; and the Asn, Ser, Thr or Hyp residues may be glycosylated. The halogen may be iodo, chloro, fluoro or bromo; preferably iodo for halogen substituted-Tyr and bromo for halogen-substituted Trp. The Tyr residues may also

be substituted with the 3-hydroxyl or 2-hydroxyl isomers (meta-Tyr or ortho-Tyr, respectively) and corresponding O-sulpho- and O-phospho-derivatives. The acidic amino acid residues may be substituted with any synthetic acidic amino acid, e.g., tetrazolyl derivatives of Gly and Ala. The aliphatic amino acids may be substituted by synthetic derivatives bearing non-natural aliphatic  
 5 branched or linear side chains  $C_nH_{2n+2}$  up to and including  $n=8$ . The Leu residues may be substituted with Leu (D). The Glu residues may be substituted with Glu. The Glu residues may be substituted with Glu. The Met residues may be substituted with norleucine (Nle). The Cys residues may be in D or L configuration and may optionally be substituted with homocysteine (D or L).

Examples of synthetic aromatic amino acid include, but are not limited to, nitro-Phe, 4-substituted-Phe wherein the substituent is  $C_1$ - $C_3$  alkyl, carboxyl, hydroxymethyl, sulphomethyl,  
 10 halo, phenyl, -CHO, -CN, -SO<sub>3</sub>H and -NHAc. Examples of synthetic hydroxy containing amino acid, include, but are not limited to, such as 4-hydroxymethyl-Phe, 4-hydroxyphenyl-Gly, 2,6-dimethyl-Tyr and 5-amino-Tyr. Examples of synthetic basic amino acids include, but are not limited to, N-1-(2-pyrazolyl)-Arg, 2-(4-piperidyl)-Gly, 2-(4-piperidyl)-Ala, 2-[3-  
 15 (2S)pyrrolidinyl]-Gly and 2-[3-(2S)pyrrolidinyl]-Ala. These and other synthetic basic amino acids, synthetic hydroxy containing amino acids or synthetic aromatic amino acids are described in Building Block Index, Version 3.0 (1999 Catalog, pages 4-47 for hydroxy containing amino acids and aromatic amino acids and pages 66-87 for basic amino acids; see also [http://www.amino-](http://www.amino-acids.com)  
 20 [acids.com](http://www.amino-acids.com)), incorporated herein by reference, by and available from RSP Amino Acid Analogues, Inc., Worcester, MA. The residues containing protecting groups are deprotected using conventional techniques. Examples of synthetic acid amino acids include those derivatives bearing acidic  
 functionality, including carboxyl, phosphate, sulfonate and synthetic tetrazolyl derivatives such as described by Ornstein et al. (1993) and in U.S. Patent No. 5,331,001, each incorporated herein by  
 reference.

25 Optionally, in the peptides of the present invention, the Asn residues may be modified to contain an N-glycan and the Ser, Thr and Hyp residues may be modified to contain an O-glycan (e.g., g-N, g-S, g-T and g-Hyp). In accordance with the present invention, a glycan shall mean any N-, S- or O-linked mono-, di-, tri-, poly- or oligosaccharide that can be attached to any hydroxy,  
 amino or thiol group of natural or modified amino acids by synthetic or enzymatic methodologies  
 30 known in the art. The monosaccharides making up the glycan can include D-allose, D-altrose, D-glucose, D-mannose, D-gulose, D-idose, D-galactose, D-talose, D-galactosamine, D-glucosamine, D-N-acetyl-glucosamine (GlcNAc), D-N-acetyl-galactosamine (GalNAc), D-fucose or D-arabinose.



These saccharides may be structurally modified, e.g., with one or more O-sulfate, O-phosphate, O-acetyl or acidic groups, such as sialic acid, including combinations thereof. The glycan may also include similar polyhydroxy groups, such as D-penicillamine 2,5 and halogenated derivatives thereof or polypropylene glycol derivatives. The glycosidic linkage is beta and 1-4 or 1-3, preferably 1-3. The linkage between the glycan and the amino acid may be alpha or beta, preferably alpha and is 1-.

Core O-glycans have been described by Van de Steen et al. (1998), incorporated herein by reference. Mucin type O-linked oligosaccharides are attached to Ser or Thr (or other hydroxylated residues of the present peptides) by a GalNAc residue. The monosaccharide building blocks and the linkage attached to this first GalNAc residue define the "core glycans," of which eight have been identified. The type of glycosidic linkage (orientation and connectivities) are defined for each core glycan. Suitable glycans and glycan analogs are described further in U.S. Serial No. 09/420,797 filed 19 October 1999 and in PCT Application No. PCT/US99/24380 filed 19 October 1999 (PCT Published Application No. WO 00/23092), each incorporated herein by reference. A preferred glycan is Gal( $\beta$ 1 $\rightarrow$ 3)GalNAc( $\alpha$ 1 $\rightarrow$ ).

Optionally, in the peptides of general formula I and the specific peptides described herein, pairs of Cys residues may be replaced pairwise with isoteric lactam or ester-thioether replacements, such as Ser/(Glu or Asp), Lys/(Glu or Asp), Cys/(Glu or Asp) or Cys/Ala combinations. Sequential coupling by known methods (Barnay et al., 2000; Hruby et al., 1994; Bitan et al., 1997) allows replacement of native Cys bridges with lactam bridges. Thioether analogs may be readily synthesized using halo-Ala residues commercially available from RSP Amino Acid Analogues.

The present invention is further directed to derivatives of the above peptides and peptide derivatives which are acyclic permutations in which the cyclic permutants retain the native bridging pattern of native toxin. See, Craik et al. (2001).

In a fourth embodiment, the present invention is directed to uses of the conotoxin peptides described herein. In one aspect of this embodiment, members of the O-Superfamily conotoxins disclosed herein or a pharmaceutically acceptable salt or solvate thereof are used for regulating the flow of sodium ions through Na<sup>+</sup> channels. Disorders which can be treated using these conopeptides include multiple sclerosis, other demyelinating diseases (such as acute disseminated encephalomyelitis, optic neuromyelitis, adrenoleukodystrophy, acute transverse myelitis, progressive multifocal leukoencephalopathy), sub-acute sclerosing panencephalomyelitis (SSPE), metachromatic leukodystrophy, Pelizaeus-Merzbacher disease, spinal cord injury, botulinum toxin

poisoning, Huntington's chorea, compression and entrapment neuropathies (such as carpal tunnel syndrome, ulnar nerve palsy), cardiovascular disorders (such as cardiac arrhythmias, congestive heart failure), reactive gliosis, hyperglycemia, immunosuppression, cocaine addiction, cancer, cognitive dysfunction, disorders resulting from defects in neurotransmitter release (such as Eaton-Lambert syndrome), and reversal of the actions of curare and other neuromuscular blocking drugs.

In a second aspect of this embodiment, a method of treating disorders associated with voltage gated ion channel disorders in a subject is provided which comprises administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins described herein or a pharmaceutically acceptable salt or solvate thereof. Thus, these peptides can be used to treat neurologic disorders, such as anticonvulsant agents, or as neuroprotective agents, such as for treating stroke, or as cardiovascular agents or for the management of pain. These peptides can further be used to treat spasticity, spinal cord injury or upper motor neuron syndrome.

In a third aspect of this embodiment, a method of reducing/alleviating/decreasing the perception of pain by a subject or for inducing analgesia, particularly local analgesia, in a subject is provided which comprises administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins described herein or a pharmaceutically acceptable salt or solvate thereof.

In a fourth aspect of this embodiment, a method for activating (i.e., opening) ATP-sensitive  $K^+$  channels in a subject is provided which comprises administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins described herein or a pharmaceutically acceptable salt or solvate thereof.

In a fifth aspect of this embodiment, a method of treating disorders and conditions associated with proton-gated ion channels in a subject comprising administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins described herein or a pharmaceutically acceptable salt or solvate thereof.

Another embodiment of the invention contemplates a method of identifying compounds that mimic the therapeutic activity of the instant peptide, comprising the steps of: (a) conducting a biological assay on a test compound to determine the therapeutic activity; and (b) comparing the results obtained from the biological assay of the test compound to the results obtained from the

biological assay of the peptide. The peptide is labeled with any conventional label, preferably a radioiodine on an available Tyr. Thus, the invention is also directed to radioiodinated O-Superfamily conotoxins.

## 5 DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

The invention relates to relatively short peptides (termed O-Superfamily conotoxins herein), about 20-40 residues in length, which are naturally available in minute amounts in the venom of the cone snails or analogous to the naturally available peptides, and which preferably include three disulfide bonds.

10 The present invention, in another aspect, relates to a pharmaceutical composition comprising an effective amount of an O-Superfamily conotoxin peptide, a mutein thereof, an analog thereof, an active fragment thereof or pharmaceutically acceptable salts.

In one embodiment, such a pharmaceutical composition comprises a member of the O-Superfamily conotoxins described herein which has the capability of delaying inactivation of sodium channels. The activity of  $\delta$ -conotoxin peptides, members of the O-Superfamily, on sodium channels is described in U.S. Patent No. 5,739,276, incorporated herein by reference. The treatment of disorders according to this embodiment comprises the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention.

20 Sodium channels comprise a large and diverse group of proteins that, through maintenance of the cellular membrane potential, are fundamental in normal biological function. The therapeutic applications for compounds that regulate the flow of sodium ions through  $\text{Na}^+$  channels are far-reaching and include treatments of a wide range of disease and injury states. Disorders which can be treated using these conopeptides include multiple sclerosis, other demyelinating diseases (such as acute disseminated encephalomyelitis, optic neuromyelitis, adrenoleukodystrophy, acute transverse myelitis, progressive multifocal leukoencephalopathy), sub-acute sclerosing panencephalomyelitis (SSPE), metachromatic leukodystrophy, Pelizaeus-Merzbacher disease, spinal cord injury, botulinum toxin poisoning, Huntington's chorea, compression and entrapment neuropathies (such as carpal tunnel syndrome, ulnar nerve palsy), cardiovascular disorders (such as cardiac arrhythmias, congestive heart failure), reactive gliosis, hyperglycemia, immunosuppression, cocaine addiction, cancer, cognitive dysfunction, disorders resulting from

defects in neurotransmitter release (such as Eaton-Lambert syndrome), and reversal of the actions of curare and other neuromuscular blocking drugs.

In a second embodiment, such a pharmaceutical composition comprises a member of the O-Superfamily conotoxins described herein which has the capability of acting at voltage gated ion channels, particularly calcium channels, and are thus useful for treating a disorder or disease of a living animal body, including a human, which disorder or disease is responsive to the partial or complete blockade of voltage gated ion channels of the central nervous system. The activity of  $\omega$ -conotoxin peptides, members of the O-Superfamily, on calcium channels is described in U.S. Patent Nos. 5,587,454; 5,559,095 and 5,824,645, incorporated herein by reference. The treatment according to this embodiment comprises the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention.

Voltage-gated calcium channels are present in neurons, and in cardiac, smooth, and skeletal muscle and other excitable cells, and are known to play a variety of roles in membrane excitability, muscle contraction, and cellular secretion, such as in synaptic transmission (McCleskey). In neuronal cells, voltage-gated calcium channels have been classified by their electrophysiological as well as by their biochemical (binding) properties. Six classes of physiologically distinct calcium channels have been identified to date, namely the T, L, N, P, Q, and R-type channels.

It is well known that an accumulation of calcium (calcium overload) in the brain is seen after anoxia, ischemia, migraine and other hyperactivity periods of the brain, such as after epileptic convulsions. An uncontrolled high concentration of calcium in the cells of the central nervous system (CNS) is known to cause most of the degenerative changes connected with the above diseases. Compounds which can block the calcium channels of brain cells are therefore useful in the treatment of stroke, anoxia, ischemia, migraine, psychosis, or epilepsy, any other convulsive disorder and in the prevention of the degenerative changes connected with the same.

Compounds blocking the so called L-type calcium channels in the CNS are useful for the treatment of the above disorders by directly blocking the calcium uptake in the CNS. Further, it is well known that the so called N- and P-types of calcium channels, as well as possibly other types of calcium channels, are involved in the regulation of neurotransmitter release. Compounds blocking the N- and/or P-types of calcium channels indirectly and very powerfully prevent calcium overload in the CNS after the hyperactivity periods of the brain as described above by inhibiting the enhanced neurotransmitter release seen after such hyperactivity periods of the CNS, and especially the

neurotoxic, enhanced glutamate release after such hyperactivity periods of the CNS. Furthermore, blockers of the N- and/or P-types of calcium channels, as dependent upon the selectivity of the compound in question, inhibit the release of various other neurotransmitters such as aspartate, GABA, glycine, dopamine, serotonin and noradrenaline.

5        Thus, the pharmaceutical compositions comprising a member of the O-Superfamily conotoxins of the present invention are useful as neuroprotectants, cardiovascular agents, anticonvulsants, analgesics or adjuvants to general anesthetics. A "neurological disorder or disease" is a disorder or disease of the nervous system including, but not limited to, global and focal ischemic and hemorrhagic stroke, head trauma, spinal cord injury, hypoxia-induced nerve cell damage as in  
10       cardiac arrest or neonatal distress or epilepsy. In addition, a "neurological disorder or disease" is a disease state and condition in which a neuroprotectant, anticonvulsant, analgesic and/or as an adjunct in general anesthesia may be indicated, useful, recommended or prescribed.

15       More specifically, the present invention is directed to the use of a member of the O-Superfamily conotoxins for the treatment and alleviation of epilepsy and as a general anticonvulsant agent. The present invention is also directed to the use of these compounds for reducing neurotoxic injury associated with conditions of hypoxia, anoxia or ischemia which typically follows stroke, cerebrovascular accident, brain or spinal cord trauma, myocardial infarct, physical trauma, drowning, suffocation, perinatal asphyxia, or hypoglycemic events. The present invention is further  
20       directed to the use of O-superfamily-conotoxin peptides for treating pain, including acute and chronic pain, such as migraine, nociceptive and neuropathic pain. These peptides can further be used to treat spasticity, spinal cord injury or upper motor neuron syndrome. Other uses of these compounds are described in U.S. Patent No. 5,859,186, incorporated herein by reference.

25       A "neuroprotectant" is a compound capable of preventing the neuronal death associated with a neurological disorder or disease. An "anticonvulsant" is a compound capable of reducing convulsions produced by conditions such as simple partial seizures, complex partial seizures, status epilepticus, and trauma-induced seizures such as occur following head injury, including head surgery. An "analgesic" is a compound capable of relieving pain by altering perception of nociceptive stimuli without producing anesthesia or loss of consciousness. A "muscle relaxant" is a compound that reduces muscular tension. A "adjunct in general anesthesia" is a compound useful  
30       in conjunction with anesthetic agents in producing the loss of ability to perceive pain associated with the loss of consciousness.

The invention relates as well to methods useful for treatment of neurological disorders and diseases, including, but not limited to, global and focal ischemic and hemorrhagic stroke, head trauma, spinal cord injury, hypoxia-induced nerve cell damage such as in cardiac arrest or neonatal distress, epilepsy or other convulsive disorders without undesirable side effects.

5 Thus, in one aspect, the invention provides a method of reducing/alleviating/ decreasing the perception of pain by a subject or for inducing analgesia in a subject comprising administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins of the present invention or a pharmaceutically acceptable salt or solvate thereof. The pain may be acute, persistent, inflammatory  
10 or neuropathic pain.

In a second aspect, the invention provides a method of treating stroke, head or spinal cord trauma or injury, anoxia, hypoxia-induced nerve cell damage, ischemia, migraine, psychosis, anxiety, schizophrenia, inflammation, movement disorder, epilepsy, any other convulsive disorder or in the prevention of the degenerative changes connected with the same in a subject comprising  
15 administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins of the present invention or a pharmaceutically acceptable salt or solvate thereof.

In a third embodiment, such a pharmaceutical composition comprises a member of the O-Superfamily conotoxins described herein which is useful as a local anesthetic for treating pain.  
20 These conopeptides have long lasting anesthetic activity and are particularly useful for spinal anesthesia, either administered acutely for post-operative pain or via an intrathecal pump for severe chronic pain situations or for treatment of pain in epithelial tissue. The activity of  $\mu$ O-conotoxin peptides, members of the O-Superfamily, on sodium channels is described in U.S. Patent Application No. 09/590,386 (International Application No. PCT/US00/15779) filed on 9 June 2000,  
25 incorporated herein by reference. The treatment according to this embodiment comprises the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention.

More specifically, in one aspect, the pain results from surgical or medical procedures, and a member of the O-Superfamily conotoxins as described herein is administered to the central  
30 nervous system (CNS), e.g. to the spine for spinal analgesia. In a second aspect, the pain is in an epithelial tissue region associated with damage or loss of epithelial tissue as a result of, for example, plastic surgery, canker sores, burns, sore throats, genital lesions, upper or lower gastrointestinal

bronchoscopy or endoscopy, intubation, dermatologic abrasions or chemical skin peels, and a member of the O-Superfamily conotoxins as described herein is administered to alleviate the associated pain.

In a fourth embodiment, such a pharmaceutical composition comprises a member of the O-Superfamily conotoxins which has the capability of activating (i.e., opening) ATP-sensitive K<sup>+</sup> channels, and is thus useful for treating a disorder or disease of a living animal body, including a human, which disorder or disease is responsive to the activation of ATP-sensitive K<sup>+</sup> channels. The activity of  $\kappa$ -conotoxin peptides, members of the O-Superfamily, on sodium channels is described in U.S. Patent Application No. \_\_\_\_\_ (International Application No. PCT/US00/25827) filed on 21 September 2000, incorporated herein by reference. The treatment according to this embodiment comprises the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention. Thus the invention provides a method for treating cardiac ischemia, neuronal ischemia, ocular ischemia or asthma in a subject comprising administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins described herein or a pharmaceutically acceptable salt or solvate thereof.

In a fifth embodiment, such a pharmaceutical composition comprises a member of the O-Superfamily conotoxins which has the capability of acting on proton gated ion channels, and is thus useful for treating a disorder, disease or condition of a living animal body, including a human, which disorder, disease or condition is responsive to the partial or complete blockade of proton-gated ion channels. Since, these members of the O-Superfamily antagonize the proton-gated ion channel, they are useful as analgesics, especially for pain associated with inflammation, hematomas, cardiac or muscle ischemia, or cancer. Thus, in one aspect of the present invention, the peptides and derivatives disclosed herein are useful as analgesics, i.e., for the reduction in the perception of pain or the induction of analgesia. The treatment according to this embodiment comprises the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention.

The conotoxin peptides of the present invention are identified by isolation from *Conus* venom. Alternatively, the conotoxin peptides of the present invention are identified using recombinant DNA techniques by screening cDNA libraries of various *Conus* species using conventional techniques, such as the use of reverse-transcriptase polymerase chain reaction (RT-

PCR) or the use of degenerate probes. Primers for RT-PCR are based on conserved sequences in the signal sequence and 3' untranslated region of the conotoxin peptides genes isolated using degenerate probes. Clones which hybridize to degenerate probes are analyzed to identify those which meet minimal size requirements, i.e., clones having approximately 300 nucleotides (for a propeptide), as determined using PCR primers which flank the cDNA cloning sites for the specific cDNA library being examined. These minimal-sized clones and the clones produced by RT-PCR are then sequenced. The sequences are then examined for the presence of a peptide having the characteristics noted above for the O-Superfamily conotoxin peptides.

The conotoxin peptides described herein are sufficiently small to be chemically synthesized. General chemical syntheses for preparing the foregoing conotoxin peptides are described hereinafter. Various ones of the conotoxin peptides can also be obtained by isolation and purification from specific *Conus* species using the technique described in U.S. Patent Nos. 4,447,356 (Olivera et al., 1984); 5,514,774; 5,719,264; and 5,591,821, as well as in PCT published application WO 98/03189, the disclosures of which are incorporated herein by reference.

Although the conotoxin peptides of the present invention can be obtained by purification from cone snails, because the amounts of conotoxin peptides obtainable from individual snails are very small, the desired substantially pure conotoxin peptides are best practically obtained in commercially valuable amounts by chemical synthesis using solid-phase strategy. For example, the yield from a single cone snail may be about 10 micrograms or less of conotoxin peptide. By "substantially pure" is meant that the peptide is present in the substantial absence of other biological molecules of the same type; it is preferably present in an amount of at least about 85% purity and preferably at least about 95% purity. Chemical synthesis of biologically active conotoxin peptides depends of course upon correct determination of the amino acid sequence.

The conotoxin peptides can also be produced by recombinant DNA techniques well known in the art. Such techniques are described by Sambrook et al. (1989). A gene of interest (i.e., a gene that encodes a suitable conotoxin peptide) can be inserted into a cloning site of a suitable expression vector by using standard techniques. These techniques are well known to those skilled in the art. The expression vector containing the gene of interest may then be used to transfect the desired cell line. Standard transfection techniques such as calcium phosphate co-precipitation, DEAE-dextran transfection or electroporation may be utilized. A wide variety of host/expression vector combinations may be used to express a gene encoding a conotoxin peptide of interest. Such



combinations are well known to a skilled artisan. The peptides produced in this manner are isolated, reduced if necessary, and oxidized to form the correct disulfide bonds.

One method of forming disulfide bonds in the conotoxin peptides of the present invention is the air oxidation of the linear peptides for prolonged periods under cold room temperatures or at room temperature. This procedure results in the creation of a substantial amount of the bioactive, disulfide-linked peptides. The oxidized peptides are fractionated using reverse-phase high performance liquid chromatography (HPLC) or the like, to separate peptides having different linked configurations. Thereafter, either by comparing these fractions with the elution of the native material or by using a simple assay, the particular fraction having the correct linkage for maximum biological potency is easily determined. However, because of the dilution resulting from the presence of other fractions of less biopotency, a somewhat higher dosage may be required.

The peptides are synthesized by a suitable method, such as by exclusively solid-phase techniques, by partial solid-phase techniques, by fragment condensation or by classical solution couplings.

In conventional solution phase peptide synthesis, the peptide chain can be prepared by a series of coupling reactions in which constituent amino acids are added to the growing peptide chain in the desired sequence. Use of various coupling reagents, e.g., dicyclohexylcarbodiimide or diisopropylcarbonyldimidazole, various active esters, e.g., esters of N-hydroxyphthalimide or N-hydroxy-succinimide, and the various cleavage reagents, to carry out reaction in solution, with subsequent isolation and purification of intermediates, is well known classical peptide methodology. Classical solution synthesis is described in detail in the treatise, "Methoden der Organischen Chemie (Houben-Weyl): Synthese von Peptiden," (1974). Techniques of exclusively solid-phase synthesis are set forth in the textbook, "Solid-Phase Peptide Synthesis," (Stewart and Young, 1969), and are exemplified by the disclosure of U.S. Patent 4,105,603 (Vale et al., 1978). The fragment condensation method of synthesis is exemplified in U.S. Patent 3,972,859 (1976). Other available syntheses are exemplified by U.S. Patents No. 3,842,067 (1974) and 3,862,925 (1975). The synthesis of peptides containing  $\gamma$ -carboxyglutamic acid residues is exemplified by Rivier et al. (1987), Nishiuchi et al. (1993) and Zhou et al. (1996).

Common to such chemical syntheses is the protection of the labile side chain groups of the various amino acid moieties with suitable protecting groups which will prevent a chemical reaction from occurring at that site until the group is ultimately removed. Usually also common is the protection of an  $\alpha$ -amino group on an amino acid or a fragment while that entity reacts at the

carboxyl group, followed by the selective removal of the  $\alpha$ -amino protecting group to allow subsequent reaction to take place at that location. Accordingly, it is common that, as a step in such a synthesis, an intermediate compound is produced which includes each of the amino acid residues located in its desired sequence in the peptide chain with appropriate side-chain protecting groups linked to various ones of the residues having labile side chains.

As far as the selection of a side chain amino protecting group is concerned, generally one is chosen which is not removed during deprotection of the  $\alpha$ -amino groups during the synthesis. However, for some amino acids, e.g., His, protection is not generally necessary. In selecting a particular side chain protecting group to be used in the synthesis of the peptides, the following general rules are followed: (a) the protecting group preferably retains its protecting properties and is not split off under coupling conditions, (b) the protecting group should be stable under the reaction conditions selected for removing the  $\alpha$ -amino protecting group at each step of the synthesis, and (c) the side chain protecting group must be removable, upon the completion of the synthesis containing the desired amino acid sequence, under reaction conditions that will not undesirably alter the peptide chain.

It should be possible to prepare many, or even all, of these peptides using recombinant DNA technology. However, when peptides are not so prepared, they are preferably prepared using the Merrifield solid-phase synthesis, although other equivalent chemical syntheses known in the art can also be used as previously mentioned. Solid-phase synthesis is commenced from the C-terminus of the peptide by coupling a protected  $\alpha$ -amino acid to a suitable resin. Such a starting material can be prepared by attaching an  $\alpha$ -amino-protected amino acid by an ester linkage to a chloromethylated resin or a hydroxymethyl resin, or by an amide bond to a benzhydrylamine (BHA) resin or paramethylbenzhydrylamine (MBHA) resin. Preparation of the hydroxymethyl resin is described by Bodansky et al. (1966). Chloromethylated resins are commercially available from Bio Rad Laboratories (Richmond, CA) and from Lab. Systems, Inc. The preparation of such a resin is described by Stewart and Young (1969). BHA and MBHA resin supports are commercially available, and are generally used when the desired polypeptide being synthesized has an unsubstituted amide at the C-terminus. Thus, solid resin supports may be any of those known in the art, such as one having the formulae  $-O-CH_2$ -resin support,  $-NH$  BHA resin support, or  $-NH$ -MBHA resin support. When the unsubstituted amide is desired, use of a BHA or MBHA resin is preferred, because cleavage directly gives the amide. In case the N-methyl amide is desired, it can be generated from an N-methyl BHA resin. Should other substituted amides be desired, the teaching

of U.S. Patent No. 4,569,967 (Kornreich et al., 1986) can be used, or should still other groups than the free acid be desired at the C-terminus, it may be preferable to synthesize the peptide using classical methods as set forth in the Houben-Weyl text (1974).

5 The C-terminal amino acid, protected by Boc or Fmoc and by a side-chain protecting group, if appropriate, can be first coupled to a chloromethylated resin according to the procedure set forth in K. Horiki et al. (1978), using KF in DMF at about 60°C for 24 hours with stirring, when a peptide having free acid at the C-terminus is to be synthesized. Following the coupling of the BOC-protected amino acid to the resin support, the  $\alpha$ -amino protecting group is removed, as by using trifluoroacetic acid (TFA) in methylene chloride or TFA alone. The deprotection is carried out at  
10 a temperature between about 0°C and room temperature. Other standard cleaving reagents, such as HCl in dioxane, and conditions for removal of specific  $\alpha$ -amino protecting groups may be used as described in Schroder & Lubke (1965).

15 After removal of the  $\alpha$ -amino-protecting group, the remaining  $\alpha$ -amino- and side chain-protected amino acids are coupled step-wise in the desired order to obtain the intermediate compound defined hereinbefore, or as an alternative to adding each amino acid separately in the synthesis, some of them may be coupled to one another prior to addition to the solid phase reactor. Selection of an appropriate coupling reagent is within the skill of the art. Particularly suitable as a coupling reagent is N,N'-dicyclohexylcarbodiimide (DCC, DIC, HBTU, HATU, TBTU in the presence of HOBt or HOAt).

20 The activating reagents used in the solid phase synthesis of the peptides are well known in the peptide art. Examples of suitable activating reagents are carbodiimides, such as N,N'-diisopropylcarbodiimide and N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide. Other activating reagents and their use in peptide coupling are described by Schroder & Lubke (1965) and Kapoor (1970).

25 Each protected amino acid or amino acid sequence is introduced into the solid-phase reactor in about a twofold or more excess, and the coupling may be carried out in a medium of dimethylformamide (DMF):CH<sub>2</sub>Cl<sub>2</sub> (1:1) or in DMF or CH<sub>2</sub>Cl<sub>2</sub> alone. In cases where intermediate coupling occurs, the coupling procedure is repeated before removal of the  $\alpha$ -amino protecting group prior to the coupling of the next amino acid. The success of the coupling reaction at each stage of  
30 the synthesis, if performed manually, is preferably monitored by the ninhydrin reaction, as described by Kaiser et al. (1970). Coupling reactions can be performed automatically, as on a Beckman 990 automatic synthesizer, using a program such as that reported in Rivier et al. (1978).

After the desired amino acid sequence has been completed, the intermediate peptide can be removed from the resin support by treatment with a reagent, such as liquid hydrogen fluoride or TFA (if using Fmoc chemistry), which not only cleaves the peptide from the resin but also cleaves all remaining side chain protecting groups and also the  $\alpha$ -amino protecting group at the N-terminus if it was not previously removed to obtain the peptide in the form of the free acid. If Met is present in the sequence, the Boc protecting group is preferably first removed using trifluoroacetic acid (TFA)/ethanedithiol prior to cleaving the peptide from the resin with HF to eliminate potential S-alkylation. When using hydrogen fluoride or TFA for cleaving, one or more scavengers such as anisole, cresol, dimethyl sulfide and methylethyl sulfide are included in the reaction vessel.

Cyclization of the linear peptide is preferably affected, as opposed to cyclizing the peptide while a part of the peptido-resin, to create bonds between Cys residues. To effect such a disulfide cyclizing linkage, fully protected peptide can be cleaved from a hydroxymethylated resin or a chloromethylated resin support by ammonolysis, as is well known in the art, to yield the fully protected amide intermediate, which is thereafter suitably cyclized and deprotected. Alternatively, deprotection, as well as cleavage of the peptide from the above resins or a benzhydrylamine (BHA) resin or a methylbenzhydrylamine (MBHA), can take place at 0 °C with hydrofluoric acid (HF) or TFA, followed by oxidation as described above.

The peptides are also synthesized using an automatic synthesizer. Amino acids are sequentially coupled to an MBHA Rink resin (typically 100 mg of resin) beginning at the C-terminus using an Advanced Chemtech 357 Automatic Peptide Synthesizer. Couplings are carried out using 1,3-diisopropylcarbodiimide in N-methylpyrrolidinone (NMP) or by 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU) and diethylisopropylethylamine (DIEA). The Fmoc protecting group is removed by treatment with a 20% solution of piperidine in dimethylformamide (DMF). Resins are subsequently washed with DMF (twice), followed by methanol and NMP.

Muteins, analogs or active fragments, of the foregoing  $\alpha$ -conotoxin peptides are also contemplated here. See, e.g., Hammerland et al, Eur. J. Pharmacol., 226, pp. 239-244 (1992). Derivative muteins, analogs or active fragments of the conotoxin peptides may be synthesized according to known techniques, including conservative amino acid substitutions, such as outlined in U.S. Pat. Nos. 5,545,723 (see particularly col. 2, line 50--col. 3, line 8); 5,534,615 (see particularly col. 19, line 45--col. 22, line 33); and 5,364,769 (see particularly col. 4, line 55--col. 7, line 26), each herein incorporated by reference.

Pharmaceutical compositions containing a compound of the present invention or its pharmaceutically acceptable salts or solvates as the active ingredient can be prepared according to conventional pharmaceutical compounding techniques. See, for example, *Remington's Pharmaceutical Sciences*, 18th Ed. (1990, Mack Publishing Co., Easton, PA). Typically, an antagonistic amount of the active ingredient will be admixed with a pharmaceutically acceptable carrier. The carrier may take a wide variety of forms depending on the form of preparation desired for administration, e.g., intravenous, oral or parenteral. The compositions may further contain antioxidizing agents, stabilizing agents, preservatives and the like. For examples of delivery methods see U.S. Patent No. 5,844,077, incorporated herein by reference.

"Pharmaceutical composition" means physically discrete coherent portions suitable for medical administration. "Pharmaceutical composition in dosage unit form" means physically discrete coherent units suitable for medical administration, each containing a daily dose or a multiple (up to four times) or a sub-multiple (down to a fortieth) of a daily dose of the active compound in association with a carrier and/or enclosed within an envelope. Whether the composition contains a daily dose, or for example, a half, a third or a quarter of a daily dose, will depend on whether the pharmaceutical composition is to be administered once or, for example, twice, three times or four times a day, respectively.

The term "salt", as used herein, denotes acidic and/or basic salts, formed with inorganic or organic acids and/or bases, preferably basic salts. While pharmaceutically acceptable salts are preferred, particularly when employing the compounds of the invention as medicaments, other salts find utility, for example, in processing these compounds, or where non-medicament-type uses are contemplated. Salts of these compounds may be prepared by art-recognized techniques.

Examples of such pharmaceutically acceptable salts include, but are not limited to, inorganic and organic addition salts, such as hydrochloride, sulphates, nitrates or phosphates and acetates, trifluoroacetates, propionates, succinates, benzoates, citrates, tartrates, fumarates, maleates, methane-sulfonates, isothionates, theophylline acetates, salicylates, respectively, or the like. Lower alkyl quaternary ammonium salts and the like are suitable, as well.

As used herein, the term "pharmaceutically acceptable" carrier means a non-toxic, inert solid, semi-solid liquid filler, diluent, encapsulating material, formulation auxiliary of any type, or simply a sterile aqueous medium, such as saline. Some examples of the materials that can serve as pharmaceutically acceptable carriers are sugars, such as lactose, glucose and sucrose, starches such as corn starch and potato starch, cellulose and its derivatives such as sodium carboxymethyl

cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt, gelatin, talc; excipients such as cocoa butter and suppository waxes; oils such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols, such as propylene glycol, polyols such as glycerin, sorbitol, mannitol and polyethylene glycol; esters such as ethyl oleate and ethyl laurate, 5 agar; buffering agents such as magnesium hydroxide and aluminum hydroxide; alginic acid; pyrogen-free water; isotonic saline, Ringer's solution; ethyl alcohol and phosphate buffer solutions, as well as other non-toxic compatible substances used in pharmaceutical formulations.

Wetting agents, emulsifiers and lubricants such as sodium lauryl sulfate and magnesium stearate, as well as coloring agents, releasing agents, coating agents, sweetening, flavoring and 10 perfuming agents, preservatives and antioxidants can also be present in the composition, according to the judgment of the formulator. Examples of pharmaceutically acceptable antioxidants include, but are not limited to, water soluble antioxidants such as ascorbic acid, cysteine hydrochloride, sodium bisulfite, sodium metabisulfite, sodium sulfite, and the like; oil soluble antioxidants, such as ascorbyl palmitate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), lecithin, 15 propyl gallate, alpha-tocopherol and the like; and the metal chelating agents such as citric acid, ethylenediamine tetraacetic acid (EDTA), sorbitol, tartaric acid, phosphoric acid and the like.

For oral administration, the compounds can be formulated into solid or liquid preparations such as capsules, pills, tablets, lozenges, melts, powders, suspensions or emulsions. In preparing the compositions in oral dosage form, any of the usual pharmaceutical media may be employed, 20 such as, for example, water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents, suspending agents, and the like in the case of oral liquid preparations (such as, for example, suspensions, elixirs and solutions); or carriers such as starches, sugars, diluents, granulating agents, lubricants, binders, disintegrating agents and the like in the case of oral solid preparations (such as, for example, powders, capsules and tablets). Because of their ease in administration, tablets and 25 capsules represent the most advantageous oral dosage unit form, in which case solid pharmaceutical carriers are obviously employed. If desired, tablets may be sugar-coated or enteric-coated by standard techniques. The active agent can be encapsulated to make it stable to passage through the gastrointestinal tract while at the same time allowing for passage across the blood brain barrier. See for example, WO 96/11698.

30 For parenteral administration, the compound may be dissolved in a pharmaceutical carrier and administered as either a solution or a suspension. Illustrative of suitable carriers are water, saline, dextrose solutions, fructose solutions, ethanol, or oils of animal, vegetative or synthetic

origin. The carrier may also contain other ingredients, for example, preservatives, suspending agents, solubilizing agents, buffers and the like. When the compounds are being administered intrathecally, they may also be dissolved in cerebrospinal fluid.

A variety of administration routes are available. The particular mode selected will depend of course, upon the particular drug selected, the severity of the disease state being treated and the dosage required for therapeutic efficacy. The methods of this invention, generally speaking, may be practiced using any mode of administration that is medically acceptable, meaning any mode that produces effective levels of the active compounds without causing clinically unacceptable adverse effects. Such modes of administration include oral, rectal, sublingual, topical, nasal, transdermal or parenteral routes. The term "parenteral" includes subcutaneous, intravenous, epidural, irrigation, intramuscular, release pumps, or infusion.

For example, administration of the active agent according to this invention may be achieved using any suitable delivery means, including:

- (a) pump (see, e.g., Luer & Hatton (1993), Zimm et al. (1984) and Ettinger et al. (1978));
- (b), microencapsulation (see, e.g., U.S. Patent Nos. 4,352,883; 4,353,888; and 5,084,350);
- (c) continuous release polymer implants (see, e.g., U.S. Patent No. 4,883,666);
- (d) macroencapsulation (see, e.g., U.S. Patent Nos. 5,284,761, 5,158,881, 4,976,859 and 4,968,733 and published PCT patent applications WO92/19195, WO 95/05452);
- (e) naked or unencapsulated cell grafts to the CNS (see, e.g., U.S. Patent Nos. 5,082,670 and 5,618,531);
- (f) injection, either subcutaneously, intravenously, intra-arterially, intramuscularly, or to other suitable site; or

(g) oral administration, in capsule, liquid, tablet, pill, or prolonged release formulation.

In one embodiment of this invention, an active agent is delivered directly into the CNS, preferably to the brain ventricles, brain parenchyma, the intrathecal space or other suitable CNS location, most preferably intrathecally. This administration is preferably by a pump.

Alternatively, targeting therapies may be used to deliver the active agent more specifically to certain types of cell, by the use of targeting systems such as antibodies or cell specific ligands. Targeting may be desirable for a variety of reasons, e.g. if the agent is unacceptably toxic, or if it would otherwise require too high a dosage, or if it would not otherwise be able to enter the target cells.

The active agents, which are peptides, can also be administered in a cell based delivery system in which a DNA sequence encoding an active agent is introduced into cells designed for implantation in the body of the patient, especially in the spinal cord region. Suitable delivery systems are described in U.S. Patent No. 5,550,050 and published PCT Application Nos. WO 92/19195, WO 94/25503, WO 95/01203, WO 95/05452, WO 96/02286, WO 96/02646, WO 96/40871, WO 96/40959 and WO 97/12635. Suitable DNA sequences can be prepared synthetically for each active agent on the basis of the developed sequences and the known genetic code.

The active agent is preferably administered in a therapeutically effective amount. By a "therapeutically effective amount" or simply "effective amount" of an active compound is meant a sufficient amount of the compound to treat the desired condition at a reasonable benefit/risk ratio applicable to any medical treatment. The actual amount administered, and the rate and time-course of administration, will depend on the nature and severity of the condition being treated. Prescription of treatment, e.g. decisions on dosage, timing, etc., is within the responsibility of general practitioners or specialists, and typically takes account of the disorder to be treated, the condition of the individual patient, the site of delivery, the method of administration and other factors known to practitioners. Examples of techniques and protocols can be found in *Remington's Pharmaceutical Sciences*.

Dosage may be adjusted appropriately to achieve desired drug levels, locally or systemically. Typically the active agents of the present invention exhibit their effect at a dosage range from about 0.001 mg/kg to about 250 mg/kg, preferably from about 0.01 mg/kg to about 100 mg/kg of the active ingredient, more preferably from about 0.05 mg/kg to about 75 mg/kg. A suitable dose can be administered in multiple sub-doses per day. Typically, a dose or sub-dose may contain from about 0.1 mg to about 500 mg of the active ingredient per unit dosage form. A more preferred dosage will contain from about 0.5 mg to about 100 mg of active ingredient per unit dosage form. Dosages are generally initiated at lower levels and increased until desired effects are achieved. In the event that the response in a subject is insufficient at such doses, even higher doses (or effective higher doses by a different, more localized delivery route) may be employed to the extent that patient tolerance permits. Continuous dosing over, for example 24 hours or multiple doses per day are contemplated to achieve appropriate systemic levels of compounds.

For the treatment of pain, if the route of administration is directly to the CNS, the dosage contemplated is from about 1 ng to about 100 mg per day, preferably from about 100 ng to about 10 mg per day, more preferably from about 1 µg to about 100 µg per day. If administered



peripherally, the dosage contemplated is somewhat higher, from about 100 ng to about 1000 mg per day, preferably from about 10  $\mu$ g to about 100 mg per day, more preferably from about 100  $\mu$ g to about 10 mg per day. If the conopeptide is delivered by continuous infusion (e.g., by pump delivery, biodegradable polymer delivery or cell-based delivery), then a lower dosage is contemplated than  
5 for bolus delivery.

Advantageously, the compositions are formulated as dosage units, each unit being adapted to supply a fixed dose of active ingredients. Tablets, coated tablets, capsules, ampoules and suppositories are examples of dosage forms according to the invention.

It is only necessary that the active ingredient constitute an effective amount, i.e., such that  
10 a suitable effective dosage will be consistent with the dosage form employed in single or multiple unit doses. The exact individual dosages, as well as daily dosages, are determined according to standard medical principles under the direction of a physician or veterinarian for use humans or animals.

The pharmaceutical compositions will generally contain from about 0.0001 to 99 wt. %, preferably about 0.001 to 50 wt. %, more preferably about 0.01 to 10 wt.% of the active ingredient  
15 by weight of the total composition. In addition to the active agent, the pharmaceutical compositions and medicaments can also contain other pharmaceutically active compounds. Examples of other pharmaceutically active compounds include, but are not limited to, analgesic agents, cytokines and therapeutic agents in all of the major areas of clinical medicine. When used with other  
20 pharmaceutically active compounds, the conotoxin peptides of the present invention may be delivered in the form of drug cocktails. A cocktail is a mixture of any one of the compounds useful with this invention with another drug or agent. In this embodiment, a common administration vehicle (e.g., pill, tablet, implant, pump, injectable solution, etc.) would contain both the instant composition in combination supplementary potentiating agent. The individual drugs of the cocktail  
25 are each administered in therapeutically effective amounts. A therapeutically effective amount will be determined by the parameters described above; but, in any event, is that amount which establishes a level of the drugs in the area of body where the drugs are required for a period of time which is effective in attaining the desired effects.

30 The practice of the present invention employs, unless otherwise indicated, conventional techniques of chemistry, molecular biology, microbiology, recombinant DNA, genetics, immunology, cell biology, cell culture and transgenic biology, which are within the skill of the art.

See, e.g., Maniatis *et al.*, 1982; Sambrook *et al.*, 1989; Ausubel *et al.*, 1992; Glover, 1985; Anand, 1992; Guthrie and Fink, 1991; Harlow and Lane, 1988; Jakoby and Pastan, 1979; *Nucleic Acid Hybridization* (B. D. Hames & S. J. Higgins eds. 1984); *Transcription And Translation* (B. D. Hames & S. J. Higgins eds. 1984); *Culture Of Animal Cells* (R. I. Freshney, Alan R. Liss, Inc., 1987); *Immobilized Cells And Enzymes* (IRL Press, 1986); B. Perbal, *A Practical Guide To Molecular Cloning* (1984); the treatise, *Methods In Enzymology* (Academic Press, Inc., N.Y.); *Gene Transfer Vectors For Mammalian Cells* (J. H. Miller and M. P. Calos eds., 1987, Cold Spring Harbor Laboratory); *Methods In Enzymology*, Vols. 154 and 155 (Wu *et al.* eds.), *Immunochemical Methods In Cell And Molecular Biology* (Mayer and Walker, eds., Academic Press, London, 1987); *Handbook Of Experimental Immunology*, Volumes I-IV (D. M. Weir and C. C. Blackwell, eds., 1986); Riott, *Essential Immunology*, 6th Edition, Blackwell Scientific Publications, Oxford, 1988; Hogan *et al.*, *Manipulating the Mouse Embryo*, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986).

## EXAMPLES

The present invention is described by reference to the following Examples, which are offered by way of illustration and are not intended to limit the invention in any manner. Standard techniques well known in the art or the techniques specifically described below were utilized.

### EXAMPLE 1

#### Isolation of O-Superfamily Conotoxins

Crude venom was extracted from venom ducts (Cruz *et al.*, 1976), and the components were purified as previously described (Cartier *et al.*, 1996). The crude extract from venom ducts was purified by reverse phase liquid chromatography (RPLC) using a Vydac C<sub>18</sub> semi-preparative column (10 x 250 mm). Further purification of bioactive peaks was done on a Vydac C<sub>18</sub> analytical column (4.6 x 220 mm). The effluents were monitored at 220 nm. Peaks were collected, and aliquots were assayed for activity.

The amino acid sequence of the purified peptides were determined by standard methods. The purified peptides were reduced and alkylated prior to sequencing by automated Edman degradation on an Applied Biosystems 477A Protein Sequencer with a 120A Analyzer (DNA/Peptide Facility, University of Utah) (Martinez *et al.*, 1995; Shon *et al.*, 1994).

In accordance with this method, peptides  $\delta$ -GmVIA,  $\delta$ -PVIA,  $\delta$ -SVIE,  $\delta$ -SVIE [D1E],  $\delta$ -NgVIA,  $\delta$ -TxVIA and Israel TxVIA were obtained.

## EXAMPLE 2

### Synthesis of Conopeptides

The synthesis of conopeptides, either the mature toxins or the precursor peptides, was separately performed using conventional protection chemistry as described by Cartier et al. (1996). Briefly, the linear chains were built on Rink amide resin by Fmoc procedures with 2-(1H-benzotriol-1-yl)-1,1,3,3,-tetramethyluronium tetrafluoroborated coupling using an ABI model 430A peptide synthesizer with amino acid derivatives purchased from Bachem (Torrence CA). Orthogonal protection was used on cysteines: two cysteines were protected as the stable Cys(S-acetamidomethyl), while the other two cysteines were protected as the acid-labile Cys(S-trityl). After removal of the terminal Fmoc protecting group and cleavage of the peptides from the resins, the released peptides were precipitated by filtering the reaction mixture into -10°C methyl t-butyl ether, which removed the protecting groups except the Cys(S-acetamidomethyl). The peptides were dissolved in 0.1% TFA and 60% acetonitrile and purified by RPLC on a Vydac C<sub>18</sub> preparative column (22 x 250 mm) and eluted at a flow rate of 20 mL/min with a gradient of acetonitrile in 0.1% TFA.

The disulfide bridges in the three conopeptides were formed as described in Cartier et al. (1996). Briefly, the disulfide bridges between one pair of cysteines were formed by air oxidation which was judged to be complete by analytical RPLC. The monocyclic peptides were purified by RPLC on a Vydac C<sub>18</sub> preparative column (22 x 250 mm) and eluted with a gradient of acetonitrile in 0.1% TFA. Removal of S-acetamidomethyl groups and closure of the disulfide bridge between the other pair of cysteines was carried out simultaneously by iodine oxidation. The cyclic peptides were purified by RPLC on a Vydac C<sub>18</sub> preparative column (22 x 250 mm) and eluted with a gradient of acetonitrile in 0.1% TFA.

## EXAMPLE 3

### Isolation of DNA Encoding O-Superfamily Conotoxins

DNA coding for conotoxins described herein was isolated and cloned in accordance with conventional techniques using general procedures well known in the art, such as described in Olivera et al. (1996). Alternatively, cDNA libraries was prepared from *Conus* venom duct using

conventional techniques. DNA from single clones was amplified by conventional techniques using primers which correspond approximately to the M13 universal priming site and the M13 reverse universal priming site. Clones having a size of approximately 300-500 nucleotides were sequenced and screened for similarity in sequence to known O-Superfamily conotoxins, including the  $\delta$ -conotoxins isolated in Example 1. The DNA sequences, encoded propeptide sequences and sequences of the mature toxins are set forth in the attached Table 1. DNA sequences coding for the mature toxin can also be prepared on the basis of the DNA sequences set forth on these pages. An alignment of the conotoxins is set forth in Table 2.

**TABLE 1**

**Sequences of Mature O-Superfamily Conotoxins,  
Propeptides and DNA Encoding Propeptides**

**Name:**  $\delta$ -GmVIA  
**Species:** gloriamaris  
**Isolated:** Yes  
**Cloned:** Yes

**DNA Sequence:**

ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
 GTCACGGCTGATGACTCCGGAAATGGAATGGAGATTCTTTTTCCGAAGGCGGGTCA  
 CGAAATGGAGAACCTCGAAGTCTCTAATCGGGTCAAGCCGTGCCGTAAAGAAGGTC  
 AACTTTGTGATCCGATATTTCAAACCTGCTGCCGTGGCTGGAATTGCGTTCTTTTCTG  
 CGTCTGAAACTACCGTGATGTCTTCTCTCCCCTC (SEQ ID NO:1)

**Translation:**

MKLTCMMIVAVLFLTAWTFVTADDSGNGMEILFPKAGHEMENLEVSNRVKPCRKEGQ  
 LCDPIFQNCCRGWNCVLFV (SEQ ID NO:2)

**Toxin Sequence:**

Val-Lys-Xaa3-Cys-Arg-Lys-Xaa1-Gly-Gln-Leu-Cys-Asp-Xaa3-Ile-Phe-Gln-Asn-Cys-Cys-Arg-  
 Gly-Xaa4-Asn-Cys-Val-Leu-Phe-Cys-Val-<sup>^</sup> (SEQ ID NO:3)

**Name:**  $\delta$ -GmVIA [F15Y]  
**Species:** gloriamaris

**Toxin Sequence:**

Val-Lys-Xaa3-Cys-Arg-Lys-Xaa1-Gly-Gln-Leu-Cys-Asp-Xaa3-Ile-Xaa5-Gln-Asn-Cys-Cys-  
 Arg-Gly-Xaa4-Asn-Cys-Val-Leu-Phe-Cys-Val-<sup>^</sup> (SEQ ID NO:4)

**Name:**  $\delta$ -GmVIA [F27Y]  
**Species:** gloriamaris  
**Isolated:** No

5 **Toxin Sequence:**

Val-Lys-Xaa3-Cys-Arg-Lys-Xaa1-Gly-Gln-Leu-Cys-Asp-Xaa3-Ile-Phe-Gln-Asn-Cys-Cys-Arg-Gly-Xaa4-Asn-Cys-Val-Leu-Xaa5-Cys-Val-<sup>^</sup> (SEQ ID NO:5)

10 **Name:** Omaria9  
**Species:** omaria  
**Isolated:** No  
**Cloned:** Yes

15 **DNA Sequence:**

GAAGCTGGTACGCCTGCAGGTACCGGTCCGGAATTCCCAGGTCGACATCATCATCA  
 TCGATCCATCTGTCCATCCATCCATTCAATTCGCTGCCAGACTATAATAAACATT  
 CAAGTCTCTCTTTCTTTTGTGTCTGACAGATCGATCAGGATGTGCCGTAGAGAAGC  
 TCAACTTTGTGATCCGATTTTCAAACTGCTGCCATGGCTTGTTTTGCGTTTTGGTC  
 20 TCGTCTAAAACCTACCGTGATGTCTTCTCCTCCCCCTCTAGTAGTAGTAGGCGGCCGC  
 TCTAGAGGATCCAAGCTTACGTACGCGTGCATGCGACGTCATAGCTCTTCTATAGTG  
 TCACCTAAATTCAATTCCTGGCCGTCGTTTTACAACGTCGTGACTGGGAAAACCCT  
 GCGGTTACCCAACCTAATCGCCTTGCAGCACATCCCCCTTTCGCCAGCTGGCGTAAT  
 AGCGAAGAGGCCCCGCACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGAATGGCGA  
 25 ATGGGACGCGCCCTGTAGCGGCGCATTAT (SEQ ID NO:6)

**Translation:**

SIRMCRREAQLCDPIFQNCCHGLFCVLVCV (SEQ ID NO:7)

30 **Toxin Sequence:**

Met-Cys-Arg-Arg-Xaa1-Ala-Gln-Leu-Cys-Asp-Xaa3-Ile-Phe-Gln-Asn-Cys-Cys-His-Gly-Leu-Phe-Cys-Val-Leu-Val-Cys-Val-<sup>^</sup> (SEQ ID NO:8)

35 **Name:** Tx6.11  
**Species:** textile  
**Isolated:** No  
**Cloned:** Yes

10 **DNA Sequence:**

GGCATTACCTAAAACATCACCAAGATGAAACTGACGTGCATGATGATCGTTGCTGT  
 GCTGTTCTTGACCGCCTGGACATTCGTCACGGCTGATGACTCCAGAAATGGAATGGA  
 GAATCTTTTTCCGAAGGCAGGTCACGAAATGGAGAACCTCGAAGACTCTAAACACA  
 GGCACCAGGAGAGACCGGACACCGGCGACAAAGAAGAGATGCTGCTACAGAGACA  
 15 GGTCAAGCCGTGTCTGTAAAGAACATCA<sup>^</sup>CTTTGTGATCTGATTTTTCAAACTGCTG  
 CCGTGGCTGGTATTGCGTTGTTCTGTCTTGCACTTGAAAGCTACCTGATGTGTTCTAC  
 TCCCATC (SEQ ID NO:9)

**Translation:**

MKLT CMMIVAVLFLTAWTFVTADDSRNGMENLFPKAGHEMENLEDSKHRHQERPDGTG  
DKEEMLLQRQVKPCRKEHQLCDLIFQNCCRGWYCVVLSCT (SEQ ID NO:10)

**Toxin Sequence:**

Xaa2-Val-Lys-Xaa3-Cys-Arg-Lys-Xaa1-His-Gln-Leu-Cys-Asp-Leu-Ile-Phe-Gln-Asn-Cys-Cys-  
Arg-Gly-Xaa4-Xaa5-Cys-Val-Val-Leu-Ser-Cys-Thr-^ (SEQ ID NO:11)

**Name:** Om6.6  
**Species:** omaria  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

ATGAAACTGACGTGCCTGATGATCGTTGCCGTGCTGTCCTTGACCGGCTGGACATTC  
GTCACGGCTGATGACTCTGGAAATGGATTGGGGAATCTTTTTTCGAATGCACATCAC  
GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCGTTCCACACGAGGG  
CCCTTGTAATTGGCTTACACAAAACCTGCTGCAGTGGTTATAATTGCATCATTTTTTTC  
TGCTATAAACTACCGTGATGTCTTCTCTCCCTC (SEQ ID NO:12)

**Translation:**

MKLTCLMIVAVLSLTGWTFVTADDSGNGLGNLFSNAHHEMKNPEASKLNKRCVPHEG  
PCNWLTQNCCSGYNCHIFFCL (SEQ ID NO:13)

**Toxin Sequence:**

Cys-Val-Xaa3-His-Xaa1-Gly-Xaa3-Cys-Asn-Xaa4-Leu-Thr-Gln-Asn-Cys-Cys-Ser-Gly-Xaa5-  
Asn-Cys-Ile-Ile-Phe-Phe-Cys-Leu-^ (SEQ ID NO:14)

**Name:** Da6.2  
**Species:** dalli  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

ATGAAACTGACGTGCCTGCTGATCATTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCACGGCTGATGACTCCGGAAATGGAATGGAGAATCTTTTTCCGAAGGCACGTCA  
CGAAATGGAGAACCTCGAAGACTCTAAACACAGGCACCAGGAGAGACCGGACACG  
GGCGACAAAGAAGAGATGCTGCTACAGAGACAGGTCAAGCCGTGTCGTAAAGAAC  
ATCAACTTTGTGATCTGATTTTTCAAACTGCTGCCGTGGCTGGTATTGCTTGCTTCG  
TCCTTGATCTGAACTACCGTGATGTCTTCTCTCCCATC (SEQ ID NO:15)

**Translation:**

MKLTCLLIHIVLFLTAWTFVTADDSGNNGMENLFPKARHEMENLEDSKHRHQERPDGTG  
KEEMLLQRQVKPCRKEHQLCDLIFQNCCRGWYCLLRPCI (SEQ ID NO:16)

**Toxin Sequence:**

Xaa2-Val-Lys-Xaa3-Cys-Arg-Lys-Xaa1-His-Gln-Leu-Cys-Asp-Leu-Ile-Phe-Gln-Asn-Cys-Cys-Arg-Gly-Xaa4-Xaa5-Cys-Leu-Leu-Arg-Xaa3-Cys-Ile-^ (SEQ ID NO:17)

5

**Name:** Da6.6

**Species:** dalli

**Isolated:** No

10 **Cloned:** Yes

**DNA Sequence:**

ATGAAACTGACGTGTATGCTGATCATTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCACGGCTGATGACTCCGGAAATGGAATGGAGAATCTTTTTCCGAAGGCACGTCA  
15 CGAAATGGAGAACCTCGAAGACTCTAAACACAGGCACCAGGAGAGACCGGACACG  
GGCGACAAAGAAGAGATGCTGCTACAGAGACGGGTCAAGCCGTGCAGTGAAGAAG  
GTCAACTTTGTGATCCACTTTCTCAAACTGCTGCCGTGGCTGGCATTGCGTTCTTGT  
CTCTTGCGTCTGAAACTACCGTGATGTCTTCTCTCCCATC (SEQ ID NO:18)

20 **Translation:**

MKLTCLMLIIAVLFLTAWTFVTADDSGNGMENLFPKARHEMENLEDSKHRHQERPDTGD  
KEEMLLQRRVKPCSEEGQLCDPLSQNCCRGWHCVLVSCV (SEQ ID NO:19)

**Toxin Sequence:**

25 Val-Lys-Xaa3-Cys-Ser-Xaa1-Xaa1-Gly-Gln-Leu-Cys-Asp-Xaa3-Leu-Ser-Gln-Asn-Cys-Cys-Arg-Gly-Xaa4-His-Cys-Val-Leu-Val-Ser-Cys-Val-^ (SEQ ID NO:20)

**Name:**  $\delta$ -TxVIA

30 **Species:** textile

**Isolated:** Yes

**Cloned:** Yes

**DNA Sequence:**

35 AAACATCGCCAAGATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGAC  
CGCCTGGACATTTGCCACGGCTGATGACCCAGAAATGGATTGGGGAATCTTTTTTC  
GAATGCACATCACGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGGT  
GCAAACAAAGCGGTGAAATGTGTAATTTGTTAGACCAAACTGCTGCGACGGCTAT  
TGCATAGTACTTGTCTGCACATAAACTGCCGTGATGTCTTCTCTTCCCCTCTGTGCT  
10 ACCTGGCTTGATCTTTGATTGGCGCGTGTCTTCACTGGTTATGAACCCCCCCCCC  
CCCCCCCCCCCCCTTCCGGCTCTCTGGAGGCCTCGGGGGTTCAACATCCAAATAA  
AGTGACAG (SEQ ID NO:21)

**Translation:**

15 MKLTCLMMIVAVLFLTAWTFATADDPRNCLGNLFSNAHHEMKNPEASKLNKRWCKQS  
GEMCNLLDQNCCDGYCIVLVCT (SEQ ID NO:22)

**Toxin Sequence:**

Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Met-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Asp-Gly-  
Xaa5-Cys-Ile-Val-Leu-Val-Cys-Thr-^ (SEQ ID NO:23)

5

**Name:**  $\delta$ -TxVIA [M8J]  
**Species:** textile

**Toxin Sequence:**

10 Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Xaa6-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Asp-Gly-  
Xaa5-Cys-Ile-Val-Leu-Val-Cys-Thr-^ (SEQ ID NO:24)

**Name:** M6.4  
**Species:** magus  
**Isolated:** No  
**Cloned:** Yes

15

**DNA Sequence:**

20 ATGAAACTGACGTGTGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTT  
GCCACGGCTGATGACCCCAAGAAATGGATTGGGGAATCTTTTTTCGAATGCACATCAC  
GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGGTGCAAACAAAGCG  
GTGAAATGTGTAATTTGTTAGACCAAACTGCTGCGACGGCTATTGCATAGTACTTG  
TCTGCACATAAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:25)

25

**Translation:**

MKLTCVMIVAVLFLTAWTFATADDPRNGLGNLFSNAHHMKNPASKLNKRWCKQSG  
EMCNLLDQNCDDGYCIVLVCT (SEQ ID NO:26)

30

**Toxin Sequence:**

Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Met-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Asp-Gly-  
Xaa5-Cys-Ile-Val-Leu-Val-Cys-Thr-^ (SEQ ID NO:27)

35

**Name:** Israel TxIA  
**Species:** textile  
**Isolated:** Yes  
**Cloned:** No

10

**Toxin Sequence:**

Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Met-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Asp-Gly-  
Xaa5-Cys-Ile-Val-Phe-Val-Cys-Thr-^ (SEQ ID NO:28)

15

**Name:** Di6.2  
**Species:** distans  
**Isolated:** No



**Cloned:** Yes

**DNA Sequence:**

5 ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTT  
GCCACGGCTGATGACCCCAGAAATGGATTGGGGAATCTTTTTTCGAATGCACATCAC  
GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGGTGCAAACAAAGCG  
GTGAAATGTGTAATTTGTTAGACCAAAACTGCTGCGACGGCTATTGCATAGTACTTG  
TCTGCACATAAAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:29)

10 **Translation:**

MKLTCLMIVAVLFLTAWTFATADDPRNGLGNLFSNAHHEMKNPEASKLNKRWCKQSG  
EMCNLLDQNCDDGYCIVLVCT (SEQ ID NO:30)

**Toxin Sequence:**

15 Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Met-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Asp-Gly-  
Xaa5-Cys-Ile-Val-Leu-Val-Cys-Thr-^ (SEQ ID NO:31)

**Name:** Af6.9

20 **Species:** ammiralis

**Isolated:** No

**Cloned:** Yes

**DNA Sequence:**

25 ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTT  
GCCACGGCTGATGACCCCAGAAATGGATTGGGGAATCTTTTTTCGAATGCACATCAC  
GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGGTGCAAACAAAGCG  
GTGAAATGTGTAATTTGTTAGACCAAAACTGCTGCGAGGGCTATTGCATAGTACTTG  
TCTGCACATAAAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:32)

30

**Translation:**

MKLTTCVMIVAVLFLTAWTFATADDPRNGLGNLFSNAHHEMKNPEASKLNKRWCKQSG  
EMCNLLDQNCCEGYCIVLVCT (SEQ ID NO:33)

35 **Toxin Sequence:**

Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Met-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Xaa1-Gly-  
Xaa5-Cys-Ile-Val-Leu-Val-Cys-Thr-^ (SEQ ID NO:34)

10 **Name:** Da6.4

**Species:** dalli

**Isolated:** No

**Cloned:** Yes

15 **DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GCCACGGCTGATGACCCCAGAAATGGATTGGAGAATCTTTTTTTGAAGGCACATCA

CGAAATGAACCCCGAAGCCTCTAAGTTGAATGAGAGGTGCCTTGGTGGTGGTGAAG  
 TTTGTGATATCTTTTTTCCACAATGCTGTGGCTATTGCATTCTTCTTTTCTGCACATAA  
 AACTACCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:35)

5 **Translation:**

MKLTCVMIVAVLFLTAWTFATADDPRNGLENLFLKAHHEMNPEASKLNERCLGGGEV  
 CDIFFPQCCGYCILLFCT (SEQ ID NO:36)

**Toxin Sequence:**

10 Cys-Leu-Gly-Gly-Gly-Xaa1-Val-Cys-Asp-Ile-Phe-Phe-Xaa3-Gln-Cys-Cys-Gly-Xaa5-Cys-Ile-  
 Leu-Leu-Phe-Cys-Thr-^ (SEQ ID NO:37)

**Name:** Gm6.5  
**Species:** gloriamaris  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

20 GCTTGCACGGTGAATTTGGCTTCACAGTTTTTCCACTGTCGTCTTTGGCATCATCTGAA  
 ACATCGCCAAGATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCG  
 CCTGGACATTTGCCACGGCTGATGACCCCAAGAAATGGATTGGGGAATATTTTTTCGA  
 ATGCACATCACGAAATGAAGAATCCCGAAGCCTCTAAATTGAACAAGAGGTGCCGT  
 CTAGGGGCTGAAAGTTGTGATGTAATTTCAAAAAGTCTGCTGCCAAGGCACGTGCGT  
 25 TTTTTTCTGCTTACCATGATGTCTTCTATTCTCCTCTGTGCTACCTGGCTTGATCTTTC  
 ATTAGCGCGTGCCTTTTACTGGTTATGAACCCCTGATCCGACTCTCTGGCAGCCTC  
 GGGGGTTCAACATCCAAATAAAACGACAGCACAATGACAAA (SEQ ID NO:38)

**Translation:**

30 MKLTCMMIVAVLFLTAWTFATADDPRNGLGNIFSNAHHEMNKNPEASKLNKRCRLGAE  
 SCDVISQNCQGTCTVFFCLP (SEQ ID NO:39)

**Toxin Sequence:**

35 Cys-Arg-Leu-Gly-Ala-Xaa1-Ser-Cys-Asp-Val-Ile-Ser-Gln-Asn-Cys-Cys-Gln-Gly-Thr-Cys-Val-  
 Phe-Phe-Cys-Leu-Xaa3-^ (SEQ ID NO:40)

**Name:** Gm6.6  
**Species:** gloriamaris  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

15 GGATCCTTGCACGGTGAATTTGGCTTCACAGTTTTTCCACTGTCGTCTTTCGCATCATC  
 CAAAACATCACCAGATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTG  
 ACCGCCTGGACATTCGCCACGGCTGATGACCCCAAGAAATGGATTGGAGAACTTTT  
 TTCGAATACACATCACGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGT

GCAAACAAGCTGATGAATCTTGTAATGTATTTTCACTTGACTGCTGCACCGGCTTAT  
GCTTGGGATTCTGCGTATCGTGATGTCTTCTACTCCCCCTCTGTgCTACCTGGCTTGAT  
CTTTGATTGGCGTGTGCCTTTCATTGGTTATGAACCCCCCTGATCCGATTCTTTGGCG  
GCCTCGGGGGTTCAACATCCAAATAAAGCGACAGCACAATAAAAAA (SEQ ID

5 NO:41)

**Translation:**

MKLTMMIVAVLFLTAWTFATADDPRNGLEKLFSNTHHEMKNPEASKLNKRCKQADE  
SCNVFSLDCCTGLCLGFCVS (SEQ ID NO:42)

10

**Toxin Sequence:**

Cys-Lys-Gln-Ala-Asp-Xaa1-Ser-Cys-Asn-Val-Phe-Ser-Leu-Asp-Cys-Cys-Thr-Gly-Leu-Cys-  
Leu-Gly-Phe-Cys-Val-Ser-^ (SEQ ID NO:43)

15

**Name:** Gm6.3  
**Species:** gloriamaris  
**Isolated:** No  
**Cloned:** Yes

20

**DNA Sequence:**

ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCACCTGGACATTC  
GCCACGGCCATCACCAGGAATGGATTGGGGAATCTTTTTCCGAAGAATCATCACGA  
AATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCGTTCCATACGAGGGCC  
CTTGTAATTGGCTTACACAAAACCTGCTGCGATGAGCTATGCGTATTTTTCTGCCTAT  
AAAACCTAGCCTGATGT (SEQ ID NO:44)

25

**Translation:**

MKLTMMIVAVLFLTTWTFATAITRNLGNLFPKNHHEMKNPEASKLNKRCPYEGPC  
NWLTONCCDEL CVFFCL (SEQ ID NO:45)

30

**Toxin Sequence:**

Cys-Val-Xaa3-Xaa5-Xaa1-Gly-Xaa3-Cys-Asn-Xaa4-Leu-Thr-Gln-Asn-Cys-Cys-Asp-Xaa1-  
Leu-Cys-Val-Phe-Phe-Cys-Leu-^ (SEQ ID NO:46)

35

**Name:** M6.5  
**Species:** magus  
**Isolated:** No  
**Cloned:** Yes

40

**DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTCTTCTTGACCGTCTGGACATTC  
GCCACGGCTGATGACTCCGGAAATGGATTGGAGAACTTTTTTTCGAATGCACATCA  
CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCAAACAAGCTGAT  
GAACCTTGTGATGATTTTTCACTTGAATGCTGCACCGGCATATGTCTTGGATTCTGC  
ACGTGGTGATGTCTTCCCTCCCCTC (SEQ ID NO:47)

45

**Translation:**

MKLTCVMIVAVLFLTVWTFATADDSGNGLEKLFSNAHHEMKNPEASKLNKRCKQADE  
PCDVFSLECCTGICLGFCTW (SEQ ID NO:48)

**Toxin Sequence:**

Cys-Lys-Gln-Ala-Asp-Xaa1-Xaa3-Cys-Asp-Val-Phe-Ser-Leu-Xaa1-Cys-Cys-Thr-Gly-Ile-Cys-  
Leu-Gly-Phe-Cys-Thr-Xaa4-^ (SEQ ID NO:49)

**Name:** Tx6.2  
**Species:** textile  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

GCCTTGCACGGTGAATTTGGCTTCATAGTTTTCCACTGTCGTCTTTGGCATCATCCAA  
AACATCACCAAGATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACC  
GCCTGGACATTCGCCACGGCTGATGACTCCAGCAATGGATTGGAGAATCTTTTTTTTG  
AAGGCACATCACGAAATGAACCCCGAAGCCTCTAAGTTGAACGAGAGGTGCCTTGA  
TGCTGGTGAAGTTTGTGATATTTTTTTTCCAACATGCTGCGGCTATTGCATTCTTCTT  
TTCTGCGCATAAACTACCGTGATGTCTTCTACTCCCCTCTGTGCTACCTGGCTTGAT  
CTTTGATTGGCGCGTACCCTTCACTGGTTATGAAACCCCTGATCCAGCTCTCTGGAG  
GCCTCGGGGGTTCAACATCCAAATAAAGCGACA (SEQ ID NO:50)

**Translation:**

MKLTCMMIVAVLFLTAWTFATADDSSNGLENLFLKAHHEMNPEASKLNERCLDAGEV  
CDIFFPTCCGYCILLFCA (SEQ ID NO:51)

**Toxin Sequence:**

Cys-Leu-Asp-Ala-Gly-Xaa1-Val-Cys-Asp-Ile-Phe-Phe-Xaa3-Thr-Cys-Cys-Gly-Xaa5-Cys-Ile-  
Leu-Leu-Phe-Cys-Ala-^ (SEQ ID NO:52)

**Name:** KK-1  
**Species:** textile

**Toxin Sequence:**

Cys-Ile-Xaa1-Gln-Phe-Asp-Xaa3-Cys-Xaa1-Met-Ile-Arg-His-Thr-Cys-Cys-Val-Gly-Val-Cys-  
Phe-Leu-Met-Ala-Cys-Ile-^ (SEQ ID NO:53)

**Name:** KK-2  
**Species:** textile

**Toxin Sequence:**

Cys-Ala-Xaa3-Phe-Leu-His-Xaa3-Cys-Thr-Phe-Phe-Phe-Xaa3-Asn-Cys-Cys-Asn-Ser-Xaa5-

Cys-Val-Gln-Phe-Ile-Cys-Leu-^ (SEQ ID NO:54)

**Name:** Om6.1  
**Species:** omaria  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
 GCCACGGCTGATGACCCCAGAAATGGATTGGAGAATTTTTTTTCGAAGACACAACA  
 CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCCTAGCAGAACATG  
 AAAGTTGTAATATATTTACACAAAAGTCTGCGAAGGCGTGTGCATTTTATCTGCG  
 TACAAGCTCCAGAGTGATGTCTTCTCTCCCTC (SEQ ID NO:55)

**Translation:**

MKLTMMIVAVLFLTAWTFATADDPRNGLENFFSKTQHEMKNPEASKLNKRCLAEHE  
 TCNIFTQNCCEGVCIFICVQAPE (SEQ ID NO:56)

**Toxin Sequence:**

Cys-Leu-Ala-Xaa1-His-Xaa1-Thr-Cys-Asn-Ile-Phe-Thr-Gln-Asn-Cys-Cys-Xaa1-Gly-Val-Cys-  
 Ile-Phe-Ile-Cys-Val-Gln-Ala-Xaa3-Xaa1-^ (SEQ ID NO:57)

**Name:** Om6.3  
**Species:** omaria  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

ATGAAACTGACTGTCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTT  
 GCCACGGCTGAAGACCCCAGACATGGATTGGAGAATCTTTTTTTCGAAGGCACATCA  
 CGAAATGAAGAACCCTGAAGACTCTAAATTGGACAAGAGGTGCATTCCACATTTTG  
 ACCCTTGTGACCCGATACGCCACACCTGCTGCTTTGGCCTGTGCCTACTAATAGCCT  
 GCATCTAAAAGTCCGTGATGTCTTCTCTCCCATC (SEQ ID NO:58)

**Translation:**

MKLTVMIVAVLFLTAWTFATAEDPRHGLNLFKAHHEMKNPEDSKLDRKRCIPHFD  
 CDPHRTCCFGLCLLIACI (SEQ ID NO:59)

**Toxin Sequence:**

Cys-Ile-Xaa3-His-Phe-Asp-Xaa3-Cys-Asp-Xaa3-Ile-Arg-His-Thr-Cys-Cys-Phe-Gly-Leu-Cys-  
 Leu-Leu-Ile-Ala-Cys-Ile-^ (SEQ ID NO:60)

**Name:** Om6.4  
**Species:** omaria

**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

5 ATGAAACTGACGTGCGTGATGACCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
 GTCACGGCTGAAGACCCCAAGATGGATTGAAGAATCTTTTATCAAATGCACATAA  
 CGAAATGAAGAACCCCGAAGCCTCTACATTGAACGAGAGGTGCCTTGGGTTTGGTG  
 AAGCTTGTCTTATACTTTATTTCAGACTGCTGCGGCTATTGCGTTGGTGCTATCTGCCT  
 ATAAACTACCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:61)

10

**Translation:**

MKLTCVMTVAVLFLTAWTFVTAEDPRDGLKNLLSNAHNEMKNPEASTLNERCLGFGE  
 ACLILYSDCCGYCVGAICL (SEQ ID NO:62)

15 **Toxin Sequence:**

Cys-Leu-Gly-Phe-Gly-Xaa1-Ala-Cys-Leu-Ile-Leu-Xaa5-Ser-Asp-Cys-Cys-Gly-Xaa5-Cys-Val-  
 Gly-Ala-Ile-Cys-Leu-^ (SEQ ID NO:63)

20 **Name:** Au6.1  
**Species:** aulicus  
**Isolated:** No  
**Cloned:** Yes

25 **DNA Sequence:**

ATGAAACTGACGTGTGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
 GCCACGGCTGATGACCCCAAGAAATGGATTGGAGAATCTTTTTTCGAAGACACAACA  
 CAAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCAAAGCAGAAAAT  
 GAACTTTGTAATATATTTATACAAAACCTGCTGCGACGGGACGTGCCTTCTTATCTGC  
 30 ATACAAAATCCACAGTGATGTCTTCTCTCCTACCCTC (SEQ ID NO:64)

**Translation:**

MKLTCVMIVAVLFLTAWTFATADDPRNGLENLFSKTQHKMKNPEASKLNKRCKAENE  
 LCNIFIQNCCDGTCLLICIQNPQ (SEQ ID NO:65)

35

**Toxin Sequence:**

Cys-Lys-Ala-Xaa1-Asn-Xaa1-Leu-Cys-Asn-Ile-Phe-Ile-Gln-Asn-Cys-Cys-Asp-Gly-Thr-Cys-  
 Leu-Leu-Ile-Cys-Ile-Gln-Asn-Xaa3-Gln-^ (SEQ ID NO:66)

10

**Name:** Au6.2  
**Species:** aulicus  
**Isolated:** No  
**Cloned:** Yes

15

**DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATT

GCCACGGCTGATGACCCCAGAAATGGATTGGATAATCGTTTTTCGAAGGCACGTCA  
CGAAATGAATAACCGCAGAGCCTCTAAATTGAACAAGAGGTGCCTTGAGTTTGGTG  
AACTTTGTAATTTTTTTTTTCCCAACCTGCTGCGGCTATTGCGTTCTTCTTGCTGCCTA  
TAAACTACCGTGATGTCTTCTCTTCCCCTC (SEQ ID NO:67)

5

**Translation:**

MKLTCVMIVAVLFLTAWTFATADDPRNGLDNRFKARHEMNRRASKLNKRCLEFGE  
LCNFFFPTCCGYCVLLVCL (SEQ ID NO:68)

10 **Toxin Sequence:**

Cys-Leu-Xaa1-Phe-Gly-Xaa1-Leu-Cys-Asn-Phe-Phe-Phe-Xaa3-Thr-Cys-Cys-Gly-Xaa5-Cys-  
Val-Leu-Leu-Val-Cys-Leu-^ (SEQ ID NO:69)

15 **Name:** Da6.5  
**Species:** dalli  
**Isolated:** No  
**Cloned:** Yes

20 **DNA Sequence:**

ATGAAACTGACGTGTGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTT  
GTCATGGCTGATGACTCCGGAAATGGATTGGAAAATCTGTTTTTCGAAGGCACATCA  
CGAAATGAAGAACCCTGAAGCCTCTAAATTGAACAAGAGGTGCGCTCAAAGCAGTG  
AATTATGTGATGCGCTGGACTCAGACTGCTGCAGTGGTGTGTTGCATGGTATTTTTCT  
GCCTATAAACTGCCGTGATGTCTTCTCTATCCCCTC (SEQ ID NO:70)

25

**Translation:**

MKLTCVMIVAVLFLTAWTFVMADDSGNLENLFSKAHHEMKNPEASKLNKRCAQSSE  
LCDALDSDCCSGVCMVFFCL (SEQ ID NO:71)

30

**Toxin Sequence:**

Cys-Ala-Gln-Ser-Ser-Xaa1-Leu-Cys-Asp-Ala-Leu-Asp-Ser-Asp-Cys-Cys-Ser-Gly-Val-Cys-  
Met-Val-Phe-Phe-Cys-Leu-^ (SEQ ID NO:72)

35

**Name:** Di6.4  
**Species:** distans  
**Isolated:** No  
**Cloned:** Yes

40

**DNA Sequence:**

ATGAAACTGACGTGCGTGATGACCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCACGGCTGAAGACCCCAGAGATGGATTGAGGAATCTTTTATCGAATGCACGTCA  
TGAAATGAAGAACCCCGAAGCCTCTAAATTGAACGAGAGGTGCCTTGGGTTTGGTG  
AAGCTTGTCTTATGCTTTATTTCAGACTGCTGCAGCTATTGCGTTGGTGTCTGCCT  
ATAAACTACCGTGATGTCTTCTACTCCCATC (SEQ ID NO:73)

45

**Translation:**

MKLTCVMTVAVLFLTAWTFVTAEDPRDGLRNLLSNARHEMKNPEASKLNERCLGFGE  
 ACLMLYSDCCSYCVGAVCL (SEQ ID NO:74)

5 **Toxin Sequence:**

Cys-Leu-Gly-Phe-Gly-Xaa1-Ala-Cys-Leu-Met-Leu-Xaa5-Ser-Asp-Cys-Cys-Ser-Xaa5-Cys-Val-  
 Gly-Ala-Val-Cys-Leu-^ (SEQ ID NO:75)

10 **Name:** Pn6.2  
**Species:** pennaceus  
**Isolated:** No  
**Cloned:** Yes

15 **DNA Sequence:**

ATGAAACTGACGTGCCTGATGACCGTTGCTGTGCTGTTCTTGACCGCCTGGACATT  
 GCCACGGCTGAAGACCCCAGAAATGGATTGGAGAATCTTTTTTCGAAGGCACATCA  
 CGAAATGAAGAACCCTGAAGACTCTAAATTGGACAAGAGGTGCGTTAAATATCTTG  
 20 ACCCTTGTGACATGTTACGCCACACCTGCTGCTTTGGCCTGTGCGTACTAATAGCCT  
 GCATCTAAAACCTGCCGTGATGTCTTCTACTCCCATC (SEQ ID NO:76)

**Translation:**

25 MKLTCLMTVAVLFLTAWTFATAEDPRNGLENLFSKAHHHEMKNPEDSKLDKRCVKYLD  
 PCDMLRHTCCFGLCVLIACI (SEQ ID NO:77)

**Toxin Sequence:**

30 Cys-Val-Lys-Xaa5-Leu-Asp-Xaa3-Cys-Asp-Met-Leu-Arg-His-Thr-Cys-Cys-Phe-Gly-Leu-Cys-  
 Val-Leu-Ile-Ala-Cys-Ile-^ (SEQ ID NO:78)

**Name:** Pn6.3  
 35 **Species:** pennaceus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

10 ATGAAACTGACGTGTGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATT  
 GCCACGGCTGATGACCCCAGAAATGGATTGGGGAATCTTTTTTCGAATGCACATCAC  
 GAAATGAAGAACCCCGAAGCTTCTAAATTGAACGAGAGGTGCCTTGGGTTTGGTGA  
 AGTTTGCAATTTCTTTTTTCCAACTGCTGCAGCTATTGCGTTGCTCTTGTCTGCCTA  
 15 TAAAACCTACCGTGATGTCTTCTATTCCCTC (SEQ ID NO:79)

**Translation:**



MKLTCVMIVAVLFLTAWTFATADDPRNGLGNLFSNAHHMKNPASKLNERCLGFGE  
VCNFFFPNCCSYCVALVCL (SEQ ID NO:80)

5 **Toxin Sequence:**

Cys-Leu-Gly-Phe-Gly-Xaa1-Val-Cys-Asn-Phe-Phe-Phe-Xaa3-Asn-Cys-Cys-Ser-Xaa5-Cys-Val-  
Ala-Leu-Val-Cys-Leu-^ (SEQ ID NO:81)

10

**Name:** Pn6.4  
**Species:** pennaceus  
**Isolated:** No  
**Cloned:** Yes

15

**DNA Sequence:**

ATGAAACTGACGTGCGTGATGCTCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GCCACGGCTGATGACTCCAGCAATGGACTGGAGAATCTTTTTTCGAAGGCACATCA  
CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCATTCCACAATTTG  
ATCCTTGTGACATGGTACGTCACACTTGCTGCAAAGGGTTGTGCGTACTAATAGCCT  
GCTCTAAACTGCGTGATGTCTTCATCTCCCCTC (SEQ ID NO:82)

20

**Translation:**

MKLTCVMLVAVLFLTAWTFATADDSSNGLENLFSKAHHMKNPASKLNKRCIPQFDP  
CDMVRHTCCKGLCVLIACSKTA (SEQ ID NO:83)

25

**Toxin Sequence:**

Cys-Ile-Xaa3-Gln-Phe-Asp-Xaa3-Cys-Asp-Met-Val-Arg-His-Thr-Cys-Cys-Lys-Gly-Leu-Cys-  
Val-Leu-Ile-Ala-Cys-Ser-Lys-Thr-Ala-^ (SEQ ID NO:84)

30

3.5 **Name:** Pn6.7  
**Species:** pennaceus  
**Isolated:** No  
**Cloned:** Yes

10 **DNA Sequence:**

ATGAAACTGACGTGCTTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GCCACGGCTGATGACCCAGAAATGGATTGGAGAATTTTTTTTCGAAGACACAACA  
CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCAAAGCAGAAAGT  
GAAGCTTGTAATATAATTACACAAAAGTGTGCGACGGCAAGTGCCTTTTTTCTGC  
ATACAAATTCCAGAGTGATGTCTTCTCCTCCCATC (SEQ ID NO:85)

15

**Translation:**

MKLTCLMIVAVLFLTAWTFATADDPRNGLENFFSKTQHEMKNPEASKLNKRCKAESEA  
CNIITQNCCDGKCLFFCIQIPE (SEQ ID NO:86)

**Toxin Sequence:**

Cys-Lys-Ala-Xaa1-Ser-Xaa1-Ala-Cys-Asn-Ile-Ile-Thr-Gln-Asn-Cys-Cys-Asp-Gly-Lys-Cys-  
Leu-Phe-Phe-Cys-Ile-Gln-Ile-Xaa3-Xaa1-^ (SEQ ID NO:87)

**Name:** Omaria3  
**Species:** omaria  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

GGTCGACATCATCATCATCATCGATCCATCTGTCCATCCATCCATTCATTCATTCGCT  
GCCAGACTGTCATAAATATTCGAGTCTCTCCTTCTGTTTGTATCTGACAGATTGAAC  
AAGAGGTGCATTGACGGTGGTGAAATTTGTGATATTTTTTTTCCAAACTGCTGCAGT  
GGGTGGTGCATTATTCTCGTCTGCGCATGAAACTACCGTGATGTCTTCTACTCCCCTC  
TAGTAGTAGTAGGCGGCCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCATGCGA  
CGTCATAGCTCTTCTATAGTGTCACCTAAATTCAATTCACCTGGCCGTCGTTTTACAAC  
GTCGTGACTGGGAAAACCTGGCGTTACCCAACCTTAATCGCCTTGCAGCACATCCCC  
CTTTCGCCAGCTGGCGTAATAGCGAAGAGGCCCGCACCGATCGCCCTTCCAACAGT  
TTGCGCAGCCTGAATGGCGAATGGGACGCGCCCTGTAGCGGCGCATTAAAGCGCGGC  
GGGTGTGGTGGGTaCGCGCAGCGTGACCGGTACACTTGCCAGCGCCCTAGCGCCCCG  
TCCTTTTGCTTTCTTCCCTTCCTTTCTCGCCACCGTTCgCCCGGGGTTTTCCCGTCaAG  
CTC (SEQ ID NO:88)

**Translation:**

LNKRCIDGGEICDIFFPNCCSGWCIIIVCA (SEQ ID NO:89)

**Toxin Sequence:**

Cys-Ile-Asp-Gly-Gly-Xaa1-Ile-Cys-Asp-Ile-Phe-Phe-Xaa3-Asn-Cys-Cys-Ser-Gly-Xaa4-Cys-  
Ile-Ile-Leu-Val-Cys-Ala-^ (SEQ ID NO:90)

**Name:** Omaria1  
**Species:** omaria  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

GGTCGACATCATCATCATCGATCCATCTGTCCATCCATCCATTCATTCATTCGCTGCC  
 AGACTGTCATAAATATTCGAGTCTCTCCTTCTGTTTGTATCTGACAGATTGAACAAG  
 AGGTGCCTTGACGGTGGTGAATTTGTGGTATTTTGTTCCTCAAGCTGCTGCAGTGGG  
 5 TGGTGCATTGTTCTCGTCTGCGCATGAAACTACCGTGATGTCTTCTACTCCCCTCTAG  
 TAGTAGTAGGCGGCCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCATGCGACGT  
 CATAGCTCTTCTATAGTGTACCTAAATTCAATTCAGTGGCCGTCGTTTTACAACGTC  
 GTGACTGGGAAAACCCTGGCGTTACCCAACCTTAATCGCCTTGCAGCACATCCCCCTT  
 TCGCCAGCTGGCGTAATAGCGAAGAGGCCCGCACCGATCGCCCTTCCCAACAAGTT  
 10 GCGCAGCCTGAATGGCGAATGGGACGCGCCCTGTAGCGGCGCATTAAAGCGCGGCGG  
 GTGTGGTGGTTACGCGCACCGTGACCGCTACACTTGCCAGCGCCCTAGCCGCCCGCT  
 CCTTTCGCTTCTTCCCTTCTTCTCGCACGTTCCGGCCGGCTTCCCCGTCAAGCTCT  
 AAATCGGGGGCTTCCCTTTTA (SEQ ID NO:91)

15 **Translation:**

LNKRCLDGGEICGILFPSCCSGWCIVLVCA (SEQ ID NO:92)

**Toxin Sequence:**

20 Cys-Leu-Asp-Gly-Gly-Xaa1-Ile-Cys-Gly-Ile-Leu-Phe-Xaa3-Ser-Cys-Cys-Ser-Gly-Xaa4-Cys-  
 Ile-Val-Leu-Val-Cys-Ala-^ (SEQ ID NO:93)

25 **Name:** Marm7  
**Species:** marmoreus  
**Isolated:** No  
**Cloned:** Yes

30 **DNA Sequence:**

GGTCGACATCATCATCATCGATCCATCTGTCCATCCATCCATCCATTCATTCGCTGCC  
 AGACTGTAATAAATATTCGAGTCTCTCTTTCTGTTTGTATCTGACAGATTGAACAAG  
 AGGTGCCTTGAGTTTGGTGAAGTTTGTAAATTTTTTTTTTCCCAACCTGCTGCGGCTATT  
 35 GCGTTCTTCTTGTCTGCCTATAAAACTACCGTGATGTCTTCTACTCCCCTCTAGTAGT  
 AGTAGGCGGCCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCATGCGACGTCATA  
 GCTCTTCTATAGTGTACCTAAATTCAATTCAGTGGCCGTCGTTTTACAACGTCGTGA  
 CTGGGAAAACCCTGGCGTTACCCAACCTTAATCGCCTTGCAGCACATCCCCCTTTCGC  
 CAGCTGGCGTAATAGCGAAGAGGCCCGCACCGATCGCCCTTCCCAACAGTTGCGCA  
 10 GCCTGAATGGCGAATGGGACGCGCCCTGTAGCGGCGCATTAAAGCGCGGCGGGTGTG  
 GTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCTTTCG  
 CTTTCTTCCCTTCCCTTCTCGCCACGTTTCGCCGGCTTCCCCGTCAA (SEQ ID NO:94)

**Translation:**

15 LNKRCLEFGEVCNFFFPTCCGYCVLLVCL (SEQ ID NO:95)

**Toxin Sequence:**

Cys-Leu-Xaa1-Phe-Gly-Xaa1-Val-Cys-Asn-Phe-Phe-Phe-Xaa3-Thr-Cys-Cys-Gly-Xaa5-Cys-Val-Leu-Leu-Val-Cys-Leu-^ (SEQ ID NO:96)

5

**Name:** Marm12  
**Species:** marmoreus  
**Isolated:** No  
**Cloned:** Yes

10

**DNA Sequence:**

15

20

GAAAGCTGGTACGCCTGCAGGTACCGGTCCGGAATTCCCGGGTCGACATCATCATC  
 ATCATCGATCCATCTGTCCATCCATCCATTCATTCATTCGCTGCCAGACTGTAATAA  
 ATATTCGAGTTTCTCCTTCTGTTTGTATCTGACAGGTTGAACAAGAGGTGCCAAGAG  
 TTCGGTGAAGTTTGTAAATTTTTTTTTTCCCAGACTGCTGCGGCTATTGCGTTCTTTTAC  
 TCTGCATATAAAACTACCGTGATGTCTTCTCTTCCCATCTAGTAGTAGTAGTAGTAG  
 TAGGCGGCCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCGACGTCATAGC  
 TCTTCTATAGTGTACCTAAATTCAATTCAGTGGCCGTCGTTTTACAACCGTCGTGAC  
 TGGGAAAACCCTGGCGTTCCCAACTTAATTCGCCTTGCAGCACAT (SEQ ID NO:97)

**Translation:**

25

LNKRCQEFGEVCNFFFPDCCGYCVLLLCI (SEQ ID NO:98)

**Toxin Sequence:**

30

Cys-Gln-Xaa1-Phe-Gly-Xaa1-Val-Cys-Asn-Phe-Phe-Phe-Xaa3-Asp-Cys-Cys-Gly-Xaa5-Cys-Val-Leu-Leu-Leu-Cys-Ile-^ (SEQ ID NO:99)

**Name:** Omaria7  
**Species:** omaria  
**Isolated:** No  
**Cloned:** Yes

35

**DNA Sequence:**

40

45

TTTTGAAGCNGGTACGCCTGCAGGTACCGGTCCGGAATTCCCGGGTCGACATCATCA  
 TCATCATCGATCCATCTGTCCATCCATCCATTCATTCATTCGCTACCAGACTGTAATA  
 AATATTCGGGTCTCTCTTTCTGTTTGTATCTGACAGATTGGACAAGAGGTGCATTCC  
 ACATTTTGACCCTTGTGACCCGATACGCCACACCTGCTGCTTTGGCCTGTGCCTACT  
 AATAGCCTGCATCTAAAACTGCCGTGATGTCTTCTCCTCCCCTCTAGTAGTAGTAGG  
 CGGCCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCGACGTCATAGCTCTTC  
 TATAGTGTACCTAAATTCAATTCAGTGGCCGTCGTTTTACAACGTCGTGACTGGGA  
 AAACCCTGGCGTTACCCAACCTTAATCGCCTTGCAGCACATCCCCCTTTCGCCAGCTG

GCGTAATAGCGAAGAGGCCCCGCACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGA  
ATGGCGAATGGGACGCGCCCTGTAGCGGCGCT (SEQ ID NO:100)

**Translation:**

5 LDKRCIPHFDPDPIRHTCCFGLCLLIACI (SEQ ID NO:101)

**Toxin Sequence:**

10 Cys-Ile-Xaa3-His-Phe-Asp-Xaa3-Cys-Asp-Xaa3-Ile-Arg-His-Thr-Cys-Cys-Phe-Gly-Leu-Cys-  
Leu-Leu-Ile-Ala-Cys-Ile-^ (SEQ ID NO:102)

**Name:** Omarial1

15 **Species:** omaria

**Isolated:** No

**Cloned:** Yes

**DNA Sequence:**

20 GGTACGCCTGCAGGTACCGGTCCGGAATTCCCGGGTCGACATCATCATCGATCC  
ATCTGTCCATCCATCCATTCTTTCAATTTGCTGCCAGACTGTAATAAATATTCGAGTCT  
CTCTTTCTGTTTGTATCTGACAGATTGAACAAGAGGTGCCTTGAGTTTGGTGAAGTT  
TGTAATTTTTTTTTTCCCAACCTGCTGCGGCTATTGCGTTCTTCTTGTCTGCCTATAAA  
25 ACTACCGTGATGTCTTCTTCTTCCCCTCTAGTAGTAGTAGGCGGCCGCTCTAGAGGAT  
CCAAGCTTACGTACGCGTGCATGCGACGTCATAGCTCTTCTATAGTGTACCTAAAT  
TCAATTCACTGGCCGTCGTTTTACAACGTCGTGACTGGGAAAACCCTGGCGTTACCC  
AACTTAATCGCCTTGCAGCACATCCCCCTTTGCGCAGCTGGCGTAATAGCGAAGAGG  
30 CCCGCACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGAATGGCGAATGGGACGCG  
CCCTGTAGCGGCGCATTAAG (SEQ ID NO:103)

**Translation:**

35 LNKRCLEFGEVCNFFFPTCCGYCVLLVCL (SEQ ID NO:104)

**Toxin Sequence:**

10 Cys-Leu-Xaa1-Phe-Gly-Xaa1-Val-Cys-Asn-Phe-Phe-Phe-Xaa3-Thr-Cys-Cys-Gly-Xaa5-Cys-  
Val-Leu-Leu-Val-Cys-Leu-^ (SEQ ID NO:105)

**Name:** O6.5

**Species:** obscurus

**Isolated:** No

15 **Cloned:** Yes

**DNA Sequence:**

cgatccatctgtccatccatccattcggttcggtcgctgcccactgtaataaataaccgagtctctctgtttgtatctgacagATCGAAAA  
 AGCAATGCCGTCAAAATGGTGAAGTGTGTGATGCGAATTTGGCACACTGCTGCAGT  
 GGCCCGTGT TTTCTCTTCTGTCTAAACCAGCCGTGATGTCTTCTACTCCCCTC (SEQ  
 5 ID NO:106)

**Translation:**

VSDRSKKQCRQNGEVCDANLAHCCSGPCFLFCLNQP (SEQ ID NO:107)

**Toxin Sequence:**

Ser-Lys-Lys-Gln-Cys-Arg-Gln-Asn-Gly-Xaa1-Val-Cys-Asp-Ala-Asn-Leu-Ala-His-Cys-Cys-  
 Ser-Gly-Xaa3-Cys-Phe-Leu-Phe-Cys-Leu-Asn-Gln-Xaa3-^ (SEQ ID NO:108)

**Name:** Af6.8  
**Species:** ammiralis  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCATTGCTGTGCTGTTCTTGACCGCCTGGACATTT  
 GCCACGGCTGATGACTCCGGAAATGGATTGGAAAATCTTTTTTCGAAGGCACATCA  
 CGAAATGAAGAACCCCAAAGCCTCTAAATTGAACAAGAGGTGCACTCAAAGCGGTG  
 AACTTTGTGATGTGATAGACCCAGACTGCTGCAATAATTTTGCATTATATTTTCTG  
 CATATAAACTGCCGTGATGTCTTCTACTCCCCTC (SEQ ID NO:109)

**Translation:**

MKLTCVMIIAVLFLTAWTFATADDSGNLENLFSKAHHEMKNPKASKLNKRCTQSGEL  
 CDVIDPDCCNNFCIIFFCI (SEQ ID NO:110)

**Toxin Sequence:**

Cys-Thr-Gln-Ser-Gly-Xaa1-Leu-Cys-Asp-Val-Ile-Asp-Xaa3-Asp-Cys-Cys-Asn-Asn-Phe-Cys-  
 Ile-Ile-Phe-Phe-Cys-Ile-^ (SEQ ID NO:111)

**Name:** KK-2A  
**Species:** textile  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

GGCATTACCTAAAACATCACCAAAATGAAACTGACGTGCATGATGATCGTTGCTGT  
 GCTGTTCTTGACCGCCTGGACATTCGCCACGGCTGATGACTCCGGAAATGGATTGGA  
 GAAACTTTTTTCGAATGCACATCACGAAATGAAGAACCCCGAAGCCTCTAATTTGA  
 ACAAGAGGTGCGCTCCTTTTCTTCACCTTTGTACCTTTTCTTCCCAAAGTCTGCAA  
 5 CGGCTATTGCGTTCAATTTATCTGCCTATAAACTACTGTGATGTCTTCTATTCCCCT  
 C (SEQ ID NO:112)

**Translation:**

10 MKLTCMMIVAVLFLTAWTFATADDSGNGLEKLFSNAHHEMKNPEASNLNKRCAFLH  
 LCTFFFPNCCNGYCVQFICL (SEQ ID NO:113)

**Toxin Sequence:**

15 Cys-Ala-Xaa3-Phe-Leu-His-Leu-Cys-Thr-Phe-Phe-Phe-Xaa3-Asn-Cys-Cys-Asn-Gly-Xaa5-Cys-  
 Val-Gln-Phe-Ile-Cys-Leu-^ (SEQ ID NO:114)

**Name:** KKM1  
 20 **Species:** marmoreus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

25 GGATCCTAGCACAGTGAATTTGGCTTCACAGTTTTCCACTGTCGTCTTTGGCATCATC  
 CAAAACATCACCAAGATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTG  
 ACCGCCTGGACATTTGCCACGGCTGATGACCCAGAAATGGATTGGAGAATCTTTTT  
 TCGAAGGCACATCACGAAATGAAGAACCCCAAAGACTCTAAATTGAACAAGAGGT  
 30 GCCTTGACGCTGGTGAAATGTGTGATCTTTTAAATTCAAATGCTGCAGTGGGTGGT  
 GCATTATTCTCTTCTGCGCATAAACTACCGTGATGTCTTCTACTCCCCTCTGTGCTA  
 CCTGGCTTGATCTTTGATTGGCGCGTGCCCTTCACTGGTTATGAACCCCCCTGATCC  
 GACTCTCTGGCGGCCTCGGGGGTTCAACATCCAAATAAAGCCGACACGATACTGAC  
 GTAGAAAAAAAAAAAAAAAAAAAAAAAAAAAA (SEQ ID NO:115)

**Translation:**

MKLTCMMIVAVLFLTAWTFATADDPRNGLENLFSKAHHEMKNPKDSKLNKRCLDAGE  
 MCDLFNSKCCSGWCILFCA (SEQ ID NO:116)

**Toxin Sequence:**

15 Cys-Leu-Asp-Ala-Gly-Xaa1-Met-Cys-Asp-Leu-Phe-Asn-Ser-Lys-Cys-Cys-Ser-Gly-Xaa4-Cys-  
 Ile-Ile-Leu-Phe-Cys-Ala-^ (SEQ ID NO:117)

**Name:** KKM4  
**Species:** marmoreus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

GCCGAAAACATCACCAAGATGAAACTGACGAGCATGATGATCGTTGCTGTGCTGTT  
 CTTGACCGCCTGGACATTCGTCACGGCTGACGACTCCGGAAATGGATTGGAGAATC  
 10 TTTTTTCGAAGGCACATCACGAGATGAAGAACCCCAAAGACTCTAAATTGAACAAG  
 AGGTGCCTTGACGGTGGTGAAATTTGTGGTATTTTGTTCCTCAAGCTGCTGCAGTGGG  
 TGGTGCATTGTTCTCGTCTGCGCATGAACTACCGTGATGTCTTCTACTCCCCTCTGT  
 GCTACCTGGCTTGATCTTTGATTGGCGCGTGCCCTTCACTGGTTATGAACCCCCCTG  
 ATCCGACTCTCTGGCGGCCTCGGGGGTTCAACATCCAAATAAAGCGACACGACAAT  
 15 GACAAAAAAAAAAAAAAAAAAAAAAAAAAAAA (SEQ ID NO:118)

**Translation:**

MKLTSMIMIVAVLFLTAWTFVTADDSGNLENLFSKAHHEMKNPKDSKLNKRCLDGGE  
 20 ICGILFPSCCSGWCIVLVCA (SEQ ID NO:119)

**Toxin Sequence:**

Cys-Leu-Asp-Gly-Gly-Xaa1-Ile-Cys-Gly-Ile-Leu-Phe-Xaa3-Ser-Cys-Cys-Ser-Gly-Xaa4-Cys-  
 25 Ile-Val-Leu-Val-Cys-Ala-^ (SEQ ID NO:120)

**Name:** KKM5  
**Species:** marmoreus  
 30 **Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

GCTAGCACAGTGAATTTGGCTTCACAGTTTCCACTGTCGTCTTTGGCATCATCCAA  
 AACATCACCAAGATGAAACTGACGTGCATGATGATCGAAGCAGAGCTGTTCTTGAC  
 CGCCTGGACATTTGCCACGGCTGATGACCCAGAAATGGATTGGAGAATCTTTTTTC  
 GAAGGCACATCACGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGC  
 CCTAACACTGGTGAATTATGTGATGTGGTTGAACAAAACCTGCTGCTATACCTATTGC  
 10 TTTATTGTAGTCTGCCCTATATACTACCGTGATGTCTTCTACTCCCCTCTGTGCTGC  
 CTGGCTTGATCTTTGATTGGCGCGTGCCCTTCACTGGTTATGAACCCCCCTGATCCG  
 ACTCTCTTGCGGCCTCAGGGGTTCAACATCCAAATAAAGCGACACGAAAATGAAAA  
 AAAAAAAAAAAAAAAAAA (SEQ ID NO:121)

**Translation:**

MKLTMMIEAELFLTAWTFATADDPRNGLENLFSKAHHEMKNPEASKLNKRCPNTGEL



CDVVEQNCCYTYCFIVVCPI (SEQ ID NO:122)

### Toxin Sequence:

- 5 Cys-Xaa3-Asn-Thr-Gly-Xaa1-Leu-Cys-Asp-Val-Val-Xaa1-Gln-Asn-Cys-Cys-Xaa5-Thr-Xaa5-Cys-Phe-Ile-Val-Val-Cys-Xaa3-Ile-^ (SEQ ID NO:123)

**Name:** KKM6  
**Species:** marmoreus  
**Isolated:** No  
**Cloned:** Yes

### DNA Sequence:

15 TTGCACGGTGAATTTTCGCTTATATTTTCTACTGTCGTCTTTGGCATCATCCAAAACA  
 TCACCAAGATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCT  
 GGACATTCGTCACGGCTGTGCCTCACTCCAGCGATGTATTGGAGAATCTTTATCTGA  
 AGGCACTTCACGAAACGGAAACACGAAGCCTCTAAATTGAACGTGAGAGACGA  
 20 CGAGTGCGAACCTCCTGGAGATTTTGTGGCTTTTTTAAAATTGGGCCGCCTTGCTG  
 CAGTGGCTGGTGTCTCCTCTGGTGCGCTAAACTGCCGTGATGTCTTCTATTCCCCT  
 CTGTGCTACCTGGCTTGATCTTTGATTGGCGCGTGCCCTTCAGTGGTTATGAACCCCC  
 CTGATCCGACTCTCTGGGGGCTCGGGGGTTCAACATCCAATAAAGCTGACAACA  
 CAATAAAAAAAAAA (SEQ ID NO:124)

### Translation:

MKLTMMIVAVLFLTAWTFVTA VPHSSDVLENLYLKALHETENHEASKLNVRDDECEP  
 PGDFCGFFKIGPPCCSGWCFLWCA (SEQ ID NO:125)

### Toxin Sequence:

Asp-Asp-Xaa1-Cys-Xaa1-Xaa3-Xaa3-Gly-Asp-Phe-Cys-Gly-Phe-Phe-Lys-Ile-Gly-Xaa3-Xaa3-Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Leu-Xaa4-Cys-Ala-^ (SEQ ID NO:126)

**Name:** C. striatus S2  
**Species:** striatus  
**Isolated:** No  
**Cloned:** Yes

### DNA Sequence:

15 ATGAAACTGACGTGTGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
 GTCACGGCTGTGCCTCACTCCAGCGATGATTGGAGAATCTTTATCTGAAGGCACTT  
 CACGAAACGGAAACACGAAGCCTCTAAATTGAACGTGAGAGACGACGAGTGCG  
 AACCTCCTGGAGATTTTGTGGCTTTTTTAAAATTGGGCCGCCTTGCTGCAGTGGCT

GGTGCTTCCTCTGGTGCGCATAAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:127)

**Translation:**

MKLTCVMIVAVLFLTAWTFVTAVPHSSDALENLYLKALHETENHEASKLNVRDDECEP  
PGDFCGFFKIGPPCCSGWCFLWCA (SEQ ID NO:128)

**Toxin Sequence:**

Asp-Asp-Xaa1-Cys-Xaa1-Xaa3-Xaa3-Gly-Asp-Phe-Cys-Gly-Phe-Phe-Lys-Ile-Gly-Xaa3-Xaa3-  
Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Leu-Xaa4-Cys-Ala-^ (SEQ ID NO:129)

**Name:** Om6.5  
**Species:** omaria  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCACGGCTGTGCCTCACTCCAGCAATGCATTGGAAAATCTTTATCTGAAGGCACGT  
CACGAAATGGAAAACCCCGAAGCCTCTAAATTGAACACGAGAGACGACGATTGCG  
AACCTCCTGGAAATTTTTGTGGCATGATAAAAATTGGGCCGCCTTGCTGCAGTGGCT  
GGTGCTTTTTCGCCTGCGCCTAAAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:130)

**Translation:**

MKLTCVMIVAVLFLTAWTFVTAVPHSSNALENLYLKARHEMENPEASKLNTRDDDCEP  
PGNFCGMIKIGPPCCSGWCFFACA (SEQ ID NO:131)

**Toxin Sequence:**

Asp-Asp-Asp-Cys-Xaa1-Xaa3-Xaa3-Gly-Asn-Phe-Cys-Gly-Met-Ile-Lys-Ile-Gly-Xaa3-Xaa3-  
Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Phe-Ala-Cys-Ala-^ (SEQ ID NO:132)

**Name:** Au6.3  
**Species:** aulicus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

ATGAAACTGACGTGCCTGATGATAGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC

GTCACGGCTGTGCCTCACTCCAGCAATGCATTGGAGAATCTTTATCTGAAGGCACGT  
 CACGAAATGGAAAACCCCGAAGCCTCTAAATTGAACACGAGAGACTACGATTGCGA  
 ACCTCCTGGAAATTTTTGTGGCATGATAAAAATTGGGCCGCCCTTGCTGCAGTGGCTG  
 GTGCTTTTTCGCCTGCGCCTAAAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID

5 NO:133)

#### Translation:

10 MKLTCLMIVAVLFLTAWTFVTAVPHSSNALENLYLKARHEMENPEASKLNTRDYDCEP  
 PGNFCGMIKIGPPCCSGWCFFACA (SEQ ID NO:134)

#### Toxin Sequence:

15 Asp-Xaa5-Asp-Cys-Xaa1-Xaa3-Xaa3-Gly-Asn-Phe-Cys-Gly-Met-Ile-Lys-Ile-Gly-Xaa3-Xaa3-  
 Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Phe-Ala-Cys-Ala-^ (SEQ ID NO:135)

**Name:** Marm9  
**Species:** marmoreus  
**Isolated:** No  
**Cloned:** Yes

#### DNA Sequence:

25 GGTCGACATCATCATCATCATCGATCCATCTGTCCATCCATCTATTCATTCATTCGTG  
 GCCAAACTGTAATAAATAATGCAAGTCTCTCTTTCTGTTTGTATCTGACAGATTGAA  
 CACGAGAGACGACGATTGCGAACCTCCTGGAAATTTTTGTGGCATGATAAAAATTG  
 GGCCGCCCTTGCTGCAGTGGCTGGTGCTTTTTCGCCTGCGCCTAAAACTGCCGTGATG  
 TCTTCTCTTCCCCTCTAGTAGTAGTAGGCGGCCGCTCTAGAGGATCCAAGCTTACGT  
 30 ACGCGTGCATGCGACGTCATAGCTCTTCTATAGTGTACCTAAATTCAATTCACTGG  
 CCGTCGTTTTACAACGTCGTGACTGGGAAAACCCTGGCGTTACCCAACCTAATCGCC  
 TTGCAGCACATCCCCCTTTCGCCAGCTGGCGTAATAGCGAAGAGGCCCGCACCGAT  
 CGCCCTTCCCAACAGTTGCGCAGCCTGAATGGCGAATGGGACGCGCCCTGTAGCGG  
 CGCATTAAGCGCGGCGGGTGTGGTGGTTACGCCGCAGCCGTGACCCGCTACACTTG  
 35 CCAGCGCCCTAGCGCCCGCTCCTTTCGCTTTCTTCCTTTCTCGCCACGTTCCGCC  
 GGCTTTTCCCGTCAAGCTCTAAATCGGGGGCTCCTTTAGGGTCCGATTTAAGTGCTT  
 TAC (SEQ ID NO:136)

#### Translation:

10 LNTRDDDDCEPPGNFCGMIKIGPPCCSGWCFFACA (SEQ ID NO:137)

#### Toxin Sequence:

15 Asp-Asp-Asp-Cys-Xaa1-Xaa3-Xaa3-Gly-Asn-Phe-Cys-Gly-Met-Ile-Lys-Ile-Gly-Xaa3-Xaa3-  
 Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Phe-Ala-Cys-Ala-^ (SEQ ID NO:138)

**Name:** Rg6.4  
**Species:** regius  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

10 TTGAACCAGAGAGACTGCCTTAGTAAAAACGCTTTCTGTGCCTGGCCGATACTTGGA  
 CCACTGTGCTGCAGTGGCTGGTGCTTATACGTCTGCATGTAAAACTGCCGTGATGTC  
 TTCTATCCCCTC (SEQ ID NO:139)

**Translation:**

15 LNQRDCLSKNAFCAWPILGPLCCSGWCLYVCM (SEQ ID NO:140)

**Toxin Sequence:**

20 Asp-Cys-Leu-Ser-Lys-Asn-Ala-Phe-Cys-Ala-Xaa4-Xaa3-Ile-Leu-Gly-Xaa3-Leu-Cys-Cys-Ser-  
 Gly-Xaa4-Cys-Leu-Xaa5-Val-Cys-Met-^ (SEQ ID NO:141)

**Name:** R6.5  
**Species:** radiatus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

30 ATTGAACAAGAAAGGTGATGACTGCCTTGCTGTATAAAAAAATTGTGGCTTTCCAA  
 AACTTGAGGGCCATGCTGCAGTGGCTTGTGCTTTTTCGTCTGCGCCTAAACTGCC  
 GTGATGTCTTCTCCTCCCCT (SEQ ID NO:142)

**Translation:**

35 LNKKGDDCLAVKKNCGFPKLGGPCCSGLCFFVCA (SEQ ID NO:143)

**Toxin Sequence:**

40 Gly-Asp-Asp-Cys-Leu-Ala-Val-Lys-Lys-Asn-Cys-Gly-Phe-Xaa3-Lys-Leu-Gly-Gly-Xaa3-Cys-  
 Cys-Ser-Gly-Leu-Cys-Phe-Phe-Val-Cys-Ala-^ (SEQ ID NO:144)

45 **Name:** Rg6.2  
**Species:** regius  
**Isolated:** No

**Cloned:** Yes

**DNA Sequence:**

5 TTGAATCAGAGCGACTGCCTTCCTAGAGACACATTCTGTGCCTTGCCGCAACTTGGA  
CTACTGTGCTGCAGTGGCCGGTGCTTACTCTTCTGCGTGTA AAACTGCCGTGATGTC  
TTCTCCTCCCCTC (SEQ ID NO:145)

**Translation:**

10 LNQSDCLPRDTFCALPQLGLCCSGRCLLFCV (SEQ ID NO:146)

**Toxin Sequence:**

15 Asp-Cys-Leu-Xaa3-Arg-Asp-Thr-Phe-Cys-Ala-Leu-Xaa3-Gln-Leu-Gly-Leu-Leu-Cys-Cys-Ser-  
Gly-Arg-Cys-Leu-Leu-Phe-Cys-Val-^ (SEQ ID NO:147)

**Name:** A6.5

20 **Species:** aurisiacus

**Isolated:** No

**Cloned:** Yes

**DNA Sequence:**

25 ATGAAACTGACGTGCGTGATGACCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCACGGCTGATGACTCCAGAAATGGACTGAAGAATCTTTTCCGAAGGCACGTCA  
TGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGAGATGGGTGCTCTAATG  
CTGGTGCATTTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGATTTGCATTGTTT  
30 GGTGCACATGAGTCGTATTCTGCTGGTACATTTTGTGGCTTCAACGGAGGACTCTGC  
TGCAGCAACCTTTGCTTATTTTTCGTGTGCTTAACATATTCGTGATGTCTTCTACTCC  
CATC (SEQ ID NO:148)

**Translation:**

35 MKLTCVMTVAVLFLTAWTFVTADDSRNLKKNLFPKARHEMKNPEASKLNKRDGCSNA  
GAFCGIHPGLCCSEICIVWCT (SEQ ID NO:149)

**Toxin Sequence:**

40 Asp-Gly-Cys-Ser-Asn-Ala-Gly-Ala-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-Ile-  
Cys-Ile-Val-Xaa4-Cys-Thr-^ (SEQ ID NO:150)

45 **Name:**  $\delta$ -PVIA

**Species:** purpurascens

**Isolated:** Yes

**Cloned:** Yes

**DNA Sequence:**

5 ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACTGCCTGGACATTC  
GTCACGGCTGATGACTCCAAAAATGGACTGGAGAATCATTTTTTGGGAAGGCACGTGA  
CGAAATGAAGAACCGCGAAGCCTCTAAATTGGACAAAAAGGAAGCCTGCTATGCGC  
CTGGTACTTTTTGTGGCATAAAGCCCCGGGCTATGCTGCAGTGAGTTTTGTCTCCCGG  
GCGTCTGCTTCGGTGGTTAACTGCCGTGATGTCTTCTACTCCCCCTCTGTGCTACCTGG  
10 CTTGATCTTTGATCGGCGTGTGCCCTTCACTGGTTATGAACCCACTGATCTTACCTCT  
CTTGAAGGACCTCTGGGGTCCAGCATCCAAATAAGCGACATCCCAATGAAAAAAAAA  
AAAAAAAAAAAAAAAA (SEQ ID NO:151)

**Translation:**

15 MKLTCVMIVAVLFLTAWTFVTADDSKNGLENHFWKARDEMKNREASKLDKKEACYA  
PGTFCGIKPLGCCSEFCLPGVCFGG (SEQ ID NO:152)

**Toxin Sequence:**

20 Xaa1-Ala-Cys-Xaa5-Ala-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-  
Xaa1-Phe-Cys-Leu-Xaa3-Gly-Val-Cys-Phe-Gly-# (SEQ ID NO:153)

25 **Name:**  $\delta$ -PVIA-OH  
**Species:** purpurascens  
**Isolated:** Yes

**Toxin Sequence:**

30 Xaa1-Ala-Cys-Xaa5-Ala-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-  
Xaa1-Phe-Cys-Leu-Xaa3-Gly-Val-Cys-Phe-Gly-^ (SEQ ID NO:153)

35 **Name:**  $\delta$ -PVIA[F9A]  
**Species:** purpurascens

**Toxin Sequence:**

40 Xaa1-Ala-Cys-Xaa5-Ala-Xaa3-Gly-Thr-Ala-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-  
Xaa1-Phe-Cys-Leu-Xaa3-Gly-Val-Cys-Phe-Gly-^ (SEQ ID NO:154)

45 **Name:**  $\delta$ -PVIA[I12A]  
**Species:** purpurascens  
**Isolated:**

**Toxin Sequence:**

Xaa1-Ala-Cys-Xaa5-Ala-Xaa3-Gly-Thr-Phe-Cys-Gly-Ala-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-  
Xaa1-Phe-Cys-Leu-Xaa3-Gly-Val-Cys-Phe-Gly-^ (SEQ ID NO:155)

5

**Name:**  $\delta$ -PVIA[T8A]  
**Species:** purpurascens

10 **Toxin Sequence:**

Xaa1-Ala-Cys-Xaa5-Ala-Xaa3-Gly-Ala-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-  
Xaa1-Phe-Cys-Leu-Xaa3-Gly-Val-Cys-Phe-Gly-^ (SEQ ID NO:156)

15

**Name:** M6.3  
**Species:** magus  
**Isolated:** No  
**Cloned:** Yes

20

**DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACACCTGGACATTC  
GTCACGGCTGATGACTCCAGATATGGATTGAAGAATCTTTTCCGAAGGCACGTCAT  
25 GAAATGAAGAACCCTGAAGCCTCTAAATTGAACAAGAGAGATGGGTGCTATAATGC  
TGGTACATTTTGTGGCATCCGTCCAGGACTCTGCTGCAGCGAGTTTTGCTTTTTATGG  
TGCATAACATTTGTTGATTCTGGCTAACAGTGTGCGTTGGTTAGTGTCTTCTCCTCCC  
CTC (SEQ ID NO:157)

30 **Translation:**

MKLTCVMIVAVLFLTTWTFVTADDSRYGLKNLFPKARHEMKNPEASKLNKRDGCYNA  
GTFCGIRPGLCCSEFCFLWCITFVDSG (SEQ ID NO:158)

35 **Toxin Sequence:**

Asp-Gly-Cys-Xaa5-Asn-Ala-Gly-Thr-Phe-Cys-Gly-Ile-Arg-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-  
Phe-Cys-Phe-Leu-Xaa4-Cys-Ile-Thr-Phe-Val-Asp-Ser-# (SEQ ID NO:159)

10

**Name:** M6.6  
**Species:** magus  
**Isolated:** No  
**Cloned:** Yes

15

**DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCACCTGGACATTC  
 GTCACGGCTGATGACTCCAGATATGGATTGAAGAATCTTTTCCGAAGGCACGTCAT  
 GAAATGAAGAACCCTGAAGCCTCTAAATTGAACAAGAGAGATGAATGCTATCCTCC  
 TGGTACATTTTGTGGCATCAAACCAGGACTTTGCTGCAGCGCGATATGCTTATCGTT  
 5 TGTCTGCATATCATTGATTTTGGATTGATGTCTTCTCCTCCCCTC (SEQ ID NO:160)

**Translation:**

MKLTCVMIVAVLFLTTWTFVTADDSRYGLKNLFPKARHEMKNPEASKLNKRDECYPP  
 10 GTFCGIKPGLCCSAICLSFVCISFDF (SEQ ID NO:161)

**Toxin Sequence:**

Asp-Xaa1-Cys-Xaa5-Xaa3-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-  
 15 Ala-Ile-Cys-Leu-Ser-Phe-Val-Cys-Ile-Ser-Phe-Asp-Phe-^ (SEQ ID NO:162)

**Name:** M6.7  
**Species:** magus  
 20 **Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTACTGTTCTTGACCGCCTGGACATTC  
 25 GTCACGGCTGATGACTCCAGATATGGACTGAAGGATCTGTTTCCGAAGGAACGTCA  
 TGAAATGAAGAACCCCGAAGCCTCTAAATTGAACCAGAGAGAAGCCTGCTATAATG  
 CTGGTTCATTTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGTTTGCATTCTTTG  
 GTGCATAACATTTGTTGATTCTGGCTAACTGTGTGCGTTGGTTGATGTCTTCTCCTCC  
 30 CATC (SEQ ID NO:163)

**Translation:**

MKLTCVMIVAVLFLTAWTFVTADDSRYGLKDLFPKERHEMKNPEASKLNQREACYNA  
 35 GSFCGIHPGLCCSEFCILWCITFVDSG (SEQ ID NO:164)

**Toxin Sequence:**

Xaa1-Ala-Cys-Xaa5-Asn-Ala-Gly-Ser-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-  
 10 Phe-Cys-Ile-Leu-Xaa4-Cys-Ile-Thr-Phe-Val-Asp-Ser-# (SEQ ID NO:165)

**Name:** M6.8  
**Species:** magus  
 15 **Isolated:** No  
**Cloned:** Yes



**DNA Sequence:**

ATGAAACTGACGTGCATGATGATCGTTGCTGTACTGTTCTTGACCGCCTGGACATTC  
 GTCACGGCTGATGACTCCAGATATGGACTGAAGGATCTGTTTCCGAAGGAACGTCA  
 5 TGAAATGAAGAACCCCGAAGCCTCTAAATTGAACCAGAGAGAAGCCTGCTATAATG  
 CTGGTACATTTTGTGGCATCAAACCAGGACTTTGCTGCAGCGCGATATGCTTATCGT  
 TTGTCTGCATATCATTTGATTTTGGATTGATGTCTTCTCCTCCCCTC (SEQ ID NO:166)

**Translation:**

10 MKLTCMMIVAVLFLTAWTFVTADDSRYGLKDLFPKERHEMKNPEASKLNQREACYNA  
 GTFCGIKPGLCCSAICLSFVCISFDF (SEQ ID NO:167)

**Toxin Sequence:**

15 Xaa1-Ala-Cys-Xaa5-Asn-Ala-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-Ala-  
 Ile-Cys-Leu-Ser-Phe-Val-Cys-Ile-Ser-Phe-Asp-Phe- (SEQ ID NO:168)

20 **Name:** E6.4  
**Species:** ermineus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

25 ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACTGCCTGGACATTC  
 GTCACGGCTGATGACTCCAAAAATGGACTGGAGAATCATTTTTTGAAGGCACGTGA  
 CGAAATGAAGAACCGCGAAGCCTCTAAATTGGACAAAAAGGAAGCCTGCTATCCGC  
 30 CTGGTACTTTTTGTGGCATAAAGCCCGGGCTATGCTGCAGTGAGTTGTGTTTACCGG  
 CCGTCTGCGTCGGTGGTTAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:169)

**Translation:**

35 MKLTCVMIVAVLFLTAWTFVTADDSKNGLENHFWKARDEMKNREASKLDDKKEACYP  
 PGTFCGIKPGLCCSELCLPAVCVGG (SEQ ID NO:170)

**Toxin Sequence:**

10 Xaa1-Ala-Cys-Xaa5-Xaa3-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-  
 Xaa1-Leu-Cys-Leu-Xaa3-Ala-Val-Cys-Val-Gly-# (SEQ ID NO:171)

15 **Name:** P6.4  
**Species:** purpurascens  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

5 ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACTGCCTGGACATTC  
 GTCACGGCTGATGACTCCAAAAATGGACTGGAGAATCATTTTTGGAAGGCACGTGA  
 CGAAATGAAGAACCGCGGAAGCCTCTAAATTGGACAAAAAGGAAGCCTGCTATCCGC  
 CTGGTACTTTTTGTGGCATAAAGCCCCGGGCTATGCTGCAGTGAGTTGTGTTTACCGG  
 CCGTCTGCGTCGGTGGTAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:172)

10 **Translation:**

MKLTCMMIVAVLFLTAWTFVTADDSKNGLENHFWKARDEMKNREASKLKDKEACYP  
 PGTFCGIKPGLCCSELCLPAVCVGG (SEQ ID NO:173)

15 **Toxin Sequence:**

Xaa1-Ala-Cys-Xaa5-Xaa3-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-  
 Xaa1-Leu-Cys-Leu-Xaa3-Ala-Val-Cys-Val-Gly-# (SEQ ID NO:174)

20

**Name:**  $\delta$ -SVIE [D1E]  
**Species:** striatus  
**Isolated:** Yes  
**Cloned:** Yes

25

**DNA Sequence:**

30 ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCACTTGGACATTC  
 GTCACGGCTGATGACTCCAGATATGGATTGAAGAATCTTTTTCCGAAGGCACGTCAT  
 GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGAGAAGGGTGCTCTAGTG  
 GTGGTACATTTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGTTTGTCTTTCTTTG  
 GTGCATAACATTTATTGATTGATGTCTTCTCCTCCCCTC (SEQ ID NO:175)

**Translation:**

35

MKLTCVMIVAVLFLTTWTFVTADDSRYGLKNLFPKARHEMKNPEASKLNKREGCSSG  
 GTFCGIHPGLCCSEFCFLWCITFID (SEQ ID NO:176)

**Toxin Sequence:**

40

Xaa1-Gly-Cys-Ser-Ser-Gly-Gly-Thr-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-  
 Phe-Cys-Phe-Leu-Xaa4-Cys-Ile-Thr-Phe-Ile-Asp-^ (SEQ ID NO:177)

45

**Name:**  $\delta$ -SVIE  
**Species:** striatus  
**Isolated:** Yes

**Cloned:** Yes

**DNA Sequence:**

5 ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCACTTGGACATTC  
GTCACGGCTGATGACTCCAGATATGGATTGAAGAATCTTTTCCGAAGGCACGTCAT  
GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGAGATGGGTGCTCTAGTGG  
TGGTACATTTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGTTTGTCTTTCTTGG  
TGCATAACATTTATTGATTGATGTCTTCTCCTCCCCTC (SEQ ID NO:178)

10

**Translation:**

MKLTCVMIVAVLFLTTWTFVTADDSRYGLKNLFPKARHEMKNPEASKLNKRDGCSSG  
GTFCGIHPGLCCSEFCFLWCITFID (SEQ ID NO:179)

15

**Toxin Sequence:**

Asp-Gly-Cys-Ser-Ser-Gly-Gly-Thr-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-  
Phe-Cys-Phe-Leu-Xaa4-Cys-Ile-Thr-Phe-Ile-Asp-^ (SEQ ID NO:180)

20

**Name:**  $\delta$ -NgVIA  
**Species:** striolatus  
**Isolated:** Yes

25

**Toxin Sequence:**

Ser-Lys-Cys-Phe-Ser-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-Val-  
Arg-Cys-Phe-Ser-Leu-Phe-Cys-Ile-Ser-Phe-Xaa1-^ (SEQ ID NO:181)

30

**Name:** C6.2  
**Species:** catus  
**Isolated:** No  
**Cloned:** Yes

35

**DNA Sequence:**

10 ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCACGGCTGATGACTCCAGAAATGGACTGAAGAATCTTTTCCGAAGGCACGTCA  
TGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGATATGGGTGCTCTAATG  
CTGGTGCATTTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGCTTTGCCTGGTTT  
GGTGCACATGAGTGCTATTCTTCTGGTACATTTTGTGGCTTCAACGGAGGACTCTGC  
TGCAGCAACCTTTGCTTATTTTCGTGTGCTTAACATTTTCGTGATGTCTTCTATTCC  
15 CCTC (SEQ ID NO:182)

**Translation:**

MKLTMMIVAVLFLTAWTFVTADDSRNLKLNLFKARHEMKNPEASKLNKRYGCSNA  
GAFCGIHPGLCCSELCLVWCT (SEQ ID NO:183)

5 **Toxin Sequence:**

Xaa5-Gly-Cys-Ser-Asn-Ala-Gly-Ala-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-  
Leu-Cys-Leu-Val-Xaa4-Cys-Thr-^ (SEQ ID NO:184)

10

**Name:** C6.3  
**Species:** catus  
**Isolated:** No  
**Cloned:** Yes

15

**DNA Sequence:**

20

ATGAAACTGACGTGTATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCACGGCTGATGACTCCAGATATGGACTGAAGAATCTTTTTCCGAAGGCACGTCAT  
GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGATATGGGTGCTCTAATGC  
TGGTGCATTTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGCTTTGCCTGGGTTG  
GTGCACATGAGTGCTATTCTACTGGTACATTTTGTGGCTTCAACGGAGGACTCTGCT  
GCAGCAACCTTTGCTTATTTTCGTGTGCTTAACATTTCGTGATGTCTTCTCTATTCCC  
CTC (SEQ ID NO:185)

25

**Translation:**

MKLTMMIVAVLFLTAWTFVTADDSRYGLKLNLFKARHEMKNPEASKLNKRYGCSNA  
GAFCGIHPGLCCSELCLGWCT (SEQ ID NO:186)

30

**Toxin Sequence:**

Xaa5-Gly-Cys-Ser-Asn-Ala-Gly-Ala-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-  
Leu-Cys-Leu-Gly-Xaa4-Cys-Thr-^ (SEQ ID NO:187)

35

**Name:** Di6.3  
**Species:** distans  
**Isolated:** No  
**Cloned:** Yes

10

**DNA Sequence:**

15

ATGAAACTGACGTGTCTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCACGGCTGATGACTCCAGAAATGGATTGGAGAATCTCTCTCCGAAGGCACCTCA  
CGAAATGAAGAACCCCGAAGCCTCTAAATCGAACAAGAGATATGAGTGCTATCTAC  
TGGTACATTTTTGTGGCATCAACGGAGGACTCTGCTGCAGCAACCTTTGCTTATTTT

CGTGTGCTTAACATTTTCGTGATGTCTTCTCCTCCCATC (SEQ ID NO:188)

**Translation:**

- 5 MKLTCLMIVAVLFLTAWTFVTADDSRNGLENLSPKAPHEMKNPEASKSNKRYECYLLV  
HFCGINGGLCCSNLCLFFVCLTFS (SEQ ID NO:189)

**Toxin Sequence:**

- 10 Xaa5-Xaa1-Cys-Xaa5-Leu-Leu-Val-His-Phe-Cys-Gly-Ile-Asn-Gly-Gly-Leu-Cys-Cys-Ser-Asn-  
Leu-Cys-Leu-Phe-Phe-Val-Cys-Leu-Thr-Phe-Ser-^ (SEQ ID NO:190)

**Name:** Rg6.1  
**Species:** regius  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

- 20 TTGAGCAAGAGAGACTGCCTTCCTGACTACACGATTTGTGCCTTCAATATGGGTCTG  
TGCTGCAGCGACAAGTGCATGCTCGTCTGCCTGCCGTGATGTCTTCTCCTCCCCTC  
(SEQ ID NO:191)

**Translation:**

LSKRDCLPDYTICAFNMGLCCSDKCMLVCLP (SEQ ID NO:192)

**Toxin Sequence:**

- 30 Asp-Cys-Leu-Xaa3-Asp-Xaa5-Thr-Ile-Cys-Ala-Phe-Asn-Met-Gly-Leu-Cys-Cys-Ser-Asp-Lys-  
Cys-Met-Leu-Val-Cys-Leu-Xaa3-^ (SEQ ID NO:193)

3.5 **Name:** Rg6.3  
**Species:** regius  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

TTGAACAAGAGAATCATCTGCTTTCCTGACTACATGTTTTGTGGCGTCAATGTGTTTC  
TGTGCTGCAGTGGCAACTGCCTTCTCATCTGCGTGCCGTGATGTCTTCTACTCCCCTC  
(SEQ ID NO:194)

**Translation:**

LNKRIICFPDYMFCGVNVFLCCSGNCLLICVP (SEQ ID NO:195)

**Toxin Sequence:**

- 5 Ile-Ile-Cys-Phe-Xaa3-Asp-Xaa5-Met-Phe-Cys-Gly-Val-Asn-Val-Phe-Leu-Cys-Cys-Ser-Gly-Asn-Cys-Leu-Leu-Ile-Cys-Val-Xaa3-^ (SEQ ID NO:196)

**Name:** Gm6.2  
10 **Species:** gloriamaris  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

- 15 ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCACGGCTGTGCCTCACTCCAGCAATGCGTTGGAGAATCTTTATCTGAAGGCACAT  
CATGAAATGAACAACCCCGAAGACTCTGAATTGAACAAGAGGTGCTATGATGGTGG  
GACAGGTTGTGACTCTGGAAACCAATGCTGCAGTGGCTGGTGCATTTTCGCCTGCCT  
20 CTAAAACTGTCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:197)

**Translation:**

- 25 MKLTCMMIVAVLFLTAWTFVTAVPHSSNALENLYLKAHHEMNNPEDSELNKRCYDGG  
TGCDSGNQCCSGWCIFACL (SEQ ID NO:198)

**Toxin Sequence:**

- 30 Cys-Xaa5-Asp-Gly-Gly-Thr-Gly-Cys-Asp-Ser-Gly-Asn-Gln-Cys-Cys-Ser-Gly-Xaa4-Cys-Ile-Phe-Ala-Cys-Leu-^ (SEQ ID NO:199)

**Name:** Da6.1  
35 **Species:** dalli  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

- 10 ATGAAACTGACGTGCATTATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCACGGCTGTGCCTCACTCCAGCAATGCGTTGGAGAATCTTTATCTGAAGGCACAT  
CATGAAATGAACAACCCCGAGGACTCTGAATTGAACAAGAGGTGCTATGATGGTGG  
GACAGGTTGTGACTCTGGAAACCAATGCTGCAGTGGCTGGTGCATTTTCGTCTGCCT  
15 CTAAAACTGCCGTGATGTCTTCTCTCCCATC (SEQ ID NO:200)

**Translation:**

MKLTCIMIVAVLFLTAWTFVTA VPHSSNALENLYLKAHHEMNNPEDSELNKRCYDGGT  
GCDSGNQCCSGWCIFVCL (SEQ ID NO:201)

**Toxin Sequence:**

5

Cys-Xaa5-Asp-Gly-Gly-Thr-Gly-Cys-Asp-Ser-Gly-Asn-Gln-Cys-Cys-Ser-Gly-Xaa4-Cys-Ile-  
Phe-Val-Cys-Leu-^ (SEQ ID NO:202)

10 **Name:** Pn6.6  
**Species:** pennaceus  
**Isolated:** No  
**Cloned:** Yes

15 **DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACAGTC  
GTCACGGCTGTGCCTCACTCCAACAAGCGTTGGCGAATCTTTATCTGAAGGCACGT  
CACGAAATGAAAAACCCCGAAGCCTCTAATGTGGACAAGAGGTGCTTTGAGAGTTG  
20 GGTAGCTTGTGAGTCTCCAAAACGATGCTGCAGTCACGTGTGCCTTTTCGTCTGCAC  
CTGAAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:203)

**Translation:**

25 MKLTCVMIVAVLFLTAWTVVTA VPHSNKRLANLYLKARHEMKNPEASNVDKRCFESW  
VACESPKRCCSHVCLFVCT (SEQ ID NO:204)

**Toxin Sequence:**

30 Cys-Phe-Xaa1-Ser-Xaa4-Val-Ala-Cys-Xaa1-Ser-Xaa3-Lys-Arg-Cys-Cys-Ser-His-Val-Cys-Leu-  
Phe-Val-Cys-Thr-^ (SEQ ID NO:205)

35 **Name:** Di6.5  
**Species:** distans  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

40 ATGAAACTGACGTGTATGTTGATCATCGCTGTGCTGTTCTTGACGGCCTGTCAACTC  
TCTACAAATGCGAGTTACGCCAGAAGTAAGCAGAAGCATCGTGTTCTGAGGTGAC  
TGACAAAACTCCAAGTTGACCCAGCGTTGCAATGAAGCTCAAGAACATTGCACTC  
AAAATCCTGACTGCTGCAGTGAGTCTTGCAATAAGTTTGTCGGCAGATGCTTGTCAG  
15 ACTGATCTGATGTCTTCTCCTCCCATC (SEQ ID NO:206)

**Translation:**

MKLTCLMIIAVLFLTACQLSTNASYARSKQKHRVLRSTDKNSKLTQRCNEAQEHCTQN  
PDCCSESCNKFVGRCLSD (SEQ ID NO:207)

5 **Toxin Sequence:**

Cys-Asn-Xaa1-Ala-Gln-Xaa1-His-Cys-Thr-Gln-Asn-Xaa3-Asp-Cys-Cys-Ser-Xaa1-Ser-Cys-  
Asn-Lys-Phe-Val-Gly-Arg-Cys-Leu-Ser-Asp-^ (SEQ ID NO:208)

10

**Name:** Af6.10  
**Species:** ammiralis  
**Isolated:** No  
**Cloned:** Yes

15

**DNA Sequence:**

20

ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCACGGCTGTGCCTGACTCCAGCAATGCGTTGGAGAATCTTTATCTGAAGGCACAT  
CATGAAATGAACAACCCCGAAGACTCTGAATTGAACAAGAGGTGCTATGATGGTGG  
GACAAGTTGTAACACTGGAAACCAATGCTGCAGTGGCTGGTGCATTTTCCTCTGCCT  
CTAAAACTGCCGTGATGTCTTCTCTTCCCCTC (SEQ ID NO:209)

25

**Translation:**

MKLTCLMIVAVLFLTAWTFVTAVPDSSNALENLYLKAHHEMNPNPEDSELNKRCDGG  
TSCNTGNQCCSGWCIFLCL (SEQ ID NO:210)

30

**Toxin Sequence:**

Cys-Xaa5-Asp-Gly-Gly-Thr-Ser-Cys-Asn-Thr-Gly-Asn-Gln-Cys-Cys-Ser-Gly-Xaa4-Cys-Ile-  
Phe-Leu-Cys-Leu-^ (SEQ ID NO:211)

35

**Name:** Tx6.10  
**Species:** textile  
**Isolated:** No  
**Cloned:** Yes

10

**DNA Sequence:**

15

GGCATTACCTAAAACATCACCAAGATGAAACTGACGTGCATGATGATCGTTGCTGT  
GCTGTTCTTGACCGCCTGGACATTCGTCACGGCTGCGCCTCACTCCAGCAATGCGTT  
GGAGAATCTTTATCTGAAGGCACATCATGAAATGAACAACCCCGAAGCCTCTGAAT  
TGAACAAGAGGTGCTATGATAGTGGGACAAGTTGTAACACTGGAAACCAATGCTGC  
AGTGGCTGGTGCATTTTCGTCTCTTGCCCTCTAAAACTACCGTGATGTCTTCTCTCCC  
CTC (SEQ ID NO:212)



**Translation:**

5 MKLTCMMIVAVLFLTAWTFVTAAPHSSNALENLYLKAHHEMNNPEASELNKRCYDSG  
TSCNTGNQCCSGWCIFVSCL (SEQ ID NO:213)

**Toxin Sequence:**

10 Cys-Xaa5-Asp-Ser-Gly-Thr-Ser-Cys-Asn-Thr-Gly-Asn-Gln-Cys-Cys-Ser-Gly-Xaa4-Cys-Ile-  
Phe-Val-Ser-Cys-Leu-^ (SEQ ID NO:214)

**Name:** Gm6.4  
**Species:** gloriamaris  
15 **Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

20 ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACAGCCTGGACGCTA  
GTCATGGCTGATGACTCCAACAATGGACTGGCGAATCTTTTTTCGAAATCACGTGAC  
GAAATGGAGGACCCCGAAGCTTCTAAATTGGAGAAAAGGGATTGCCAAGCACTATG  
GGATTATTGTCCAGTACCGCTCTTGTCATCGGGTGATTGCTGCTATGGCTTAATCTGT  
25 GGCCCTTTCGTCTGCATTGGATGGTGATGTCTTCTACTCCCATC (SEQ ID NO:215)

**Translation:**

30 MKLTCMMIVAVLFLTAWTLVMADDSNNGLANLFSKSRDEMEDPEASKLEKRDCQAL  
WDYCPVPLLSSGDCCYGLICGPFVCIGW (SEQ ID NO:216)

**Toxin Sequence:**

35 Asp-Cys-Gln-Ala-Leu-Xaa4-Asp-Xaa5-Cys-Xaa3-Val-Xaa3-Leu-Leu-Ser-Ser-Gly-Asp-Cys-  
Cys-Xaa5-Gly-Leu-Ile-Cys-Gly-Xaa3-Phe-Val-Cys-Ile-Gly-Xaa4-^ (SEQ ID NO:217)

**Name:** Om6.2  
**Species:** omaria  
**Isolated:** No  
40 **Cloned:** Yes

**DNA Sequence:**

45 ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCATGGCTGATGACTCCAACAATGACTGGCAAATCTTTTCTCGAAATCACGTGAC  
GAAATGGAGGATACCGATCCTTCTAAATTGGAGAACAGAAAACTTGCCAAAGAAG  
GTGGGATTTTGTCCAGGATCGCTCGTTGGAGTGATAACTTGCTGCGGTGGCTTAAT

CTGTTTTCTGTTCTTCTGCGTTTGATAGTGATGCTCTTCTCCTCCCCT (SEQ ID NO:218)

**Translation:**

5 MKLTCLMIVAVLFLTAWTFVMADDSNNGLANLFSKSRDEMEDTDP SKLENRKTCQRR  
WDFCPGSLVGVITCCGG LICFLFFCV (SEQ ID NO:219)

**Toxin Sequence:**

10 Lys-Thr-Cys-Gln-Arg-Arg-Xaa4-Asp-Phe-Cys-Xaa3-Gly-Ser-Leu-Val-Gly-Val-Ile-Thr-Cys-  
Cys-Gly-Gly-Leu-Ile-Cys-Phe-Leu-Phe-Phe-Cys-Val-^ (SEQ ID NO:220)

15 **Name:** Da6.3  
**Species:** dalli  
**Isolated:** No  
**Cloned:** Yes

20 **DNA Sequence:**

ATGAAACTGACGTGTGTGATGATCGTTGCTGTGCTGTTTCCTGACAGCCTGGACGCTA  
GTCATGGCTGATGACTCCAACAATGGACTGGCGAATCTTTTTTCGAAATTACGTGAC  
GAAATGGAGGACCCCGAAGGTTCTAAATTGGAGAAAAAGGATTGCCAAGAAAAAT  
25 GGGATTATTGTCCAGTACCGTTCTTGGGATCGAGGTATTGCTGCGATGGCTTTATCT  
GTCCATCTTTCTTCTGCGCTTGATAGTGATGTCTTCTCTATTCCCCTC (SEQ ID  
NO:221)

**Translation:**

30 MKLTCVMIVAVLFLTAWTLVMADDSNNGLANLFSKLRDEMEDPEG SKLEKKDCQEK  
WDYCPVPFLGSR YCCDGFICPSFFCA (SEQ ID NO:222)

**Toxin Sequence:**

35 Asp-Cys-Gln-Xaa1-Lys-Xaa4-Asp-Xaa5-Cys-Xaa3-Val-Xaa3-Phe-Leu-Gly-Ser-Arg-Xaa5-Cys-  
Cys-Asp-Gly-Phe-Ile-Cys-Xaa3-Ser-Phe-Phe-Cys-Ala-^ (SEQ ID NO:223)

40 **Name:** Da6.7  
**Species:** dalli  
**Isolated:** No  
**Cloned:** Yes

45 **DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGTTGTTTCCTGACAGCCTGGACGCTA

GTCATGGCTGATGACTCCAACAATGGACTGGCGAATCATT TTTTGGAAATCACGTGAC  
GAAATGGAGGACCCTGAAGCTTCTAAATTGGAGAAAAGGGATTGCCAAGGCGAATG  
GGAGTTTTGTATAGTACCGGTCCTTGGATTGTGTATTGCTGCCCCCTGGCTTATCTGT  
GGCCCTTTCGTCTGCGTTGATATCTGATGTCTTCTATCCCCTC (SEQ ID NO:224)

**Translation:**

MKLTCVMIVAVLFLTAWTLVMADDSNNGLANHFWKSRDEMEDPEASKLEKRDCQGE  
WEFCIVPVLGFVYCCPWLICGPFVCVDI (SEQ ID NO:225)

**Toxin Sequence:**

Asp-Cys-Gln-Gly-Xaa1-Xaa4-Xaa1-Phe-Cys-Ile-Val-Xaa3-Val-Leu-Gly-Phe-Val-Xaa5-Cys-  
Cys-Xaa3-Xaa4-Leu-Ile-Cys-Gly-Xaa3-Phe-Val-Cys-Val-Asp-Ile-^ (SEQ ID NO:226)

**Name:** Pn6.5  
**Species:** pennaceus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

ATGAAACTGACGTGCCTGATGATCATTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCATGGCTGATGACCCCAGAGATGAACCGGAGGCACGTGACGAAATGAACCCCGC  
AGCCTCTAAATTGAACGAGAGAGGCTGCCTTGAAGTTGATTATTTTTCGCGGCATACC  
GTTTGTGAACAACGGGCTATGCTGCAGTGGCAATTGTGTTTTTGTCTGCACACCCCA  
AGGGAAGTAAACTGCTGTGATGTCTTCTCTTCCCATC (SEQ ID NO:227)

**Translation:**

MKLTCMLIIAVLFLTAWTFVMADDP RDEPEARDEMNP AASKLNERGCLEVDYFCGIPF  
VNNGLCSSGNCV FVCTPQ GK (SEQ ID NO:228)

**Toxin Sequence:**

Gly-Cys-Leu-Xaa1-Val-Asp-Xaa5-Phe-Cys-Gly-Ile-Xaa3-Phe-Val-Asn-Asn-Gly-Leu-Cys-Cys-  
Ser-Gly-Asn-Cys-Val-Phe-Val-Cys-Thr-Xaa3-Gln-# (SEQ ID NO:229)

**Name:** Marm6  
**Species:** marmoreus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

GGTCGACATCATCATCATCGATCCATCTGTCCATCCATCTGTCCATCCATCCATTTCAT  
TCATTCACTGCCAAACTGTCATAAATATTTGAGTCTCTCTTTCTGTTTTATCTGACA  
GATTGAACGAGAGAGACTGCCTTAATGTTGATTATTTTTGCGGCATACCGTTTGTGA  
ACAACGGGCTATGCTGCAGTGGCAATTGTGTTTTGTCTGCACACCCCAAGGGAAGT  
5 AAAACTGCCGTGATGTCTTCTCTTCCCCTCTAGTAGTAGTAGGCGGCCGCTCTAGAG  
GATCCAAGCTTACGTACGCGTGCATGCGACGTCATAGCTCTTCTATAGTGTACCTA  
AATTCAATTCAGTGGCCGTCCGTTTTACAACGTCGTGACTGGGAAAACCCTGGCGTT  
ACCCAACCTAATCGCCTTGCAGCACAT (SEQ ID NO:230)

10 **Translation:**

NERDCLNVDYFCGIPFVNNGLCCSGNCV FVCTPQ GK (SEQ ID NO:231)

**Toxin Sequence:**

15

Cys-Leu-Asn-Val-Asp-Xaa5-Phe-Cys-Gly-Ile-Xaa3-Phe-Val-Asn-Asn-Gly-Leu-Cys-Cys-Ser-  
Gly-Asn-Cys-Val-Phe-Val-Cys-Thr-Xaa3-Gln-# (SEQ ID NO:232)

20

**Name:** Marm15  
**Species:** marmoreus  
**Isolated:** No  
**Cloned:** Yes

25 **DNA Sequence:**

TCGACATCATCATCATCGATCCATCTGTCCATCCATCCATTTCATTTCGCTGCCAA  
ACTGTCATAAATATTTGAGTCTCTCTTTCTGTTTTATCTGACAGATTGGACAAGAGA  
GAGTGCCTGGAAGCTGATTATTATTGCGTCTTACCGTTTGTGGGCAACGGGATGTGC  
30 TGCAGTGGCATTGTGTTTTTGTCTGCATAGCCC (SEQ ID NO:233)

**Translation:**

LDKRECLEADYYCVLPFVGNGMCCSGICVFVCIAQRFKTV (SEQ ID NO:234)

35

**Toxin Sequence:**

Xaa1-Cys-Leu-Xaa1-Ala-Asp-Xaa5-Xaa5-Cys-Val-Leu-Xaa3-Phe-Val-Gly-Asn-Gly-Met-Cys-  
Cys-Ser-Gly-Ile-Cys-Val-Phe-Val-Cys-Ile-Ala-Gln-Arg-Phe-Lys-Thr-Val-^ (SEQ ID NO:235)

40

**Name:** Marm10  
**Species:** marmoreus  
**Isolated:** No  
45 **Cloned:** Yes

**DNA Sequence:**

GTACCGGTCCGGAATTCCCGGGTCGACATCATCATCATCGATCCATCTGTCCATCCA  
 TCCATCCATTCATTCATTCGCTGCCAAACTGTCATAAACATTTGAGTCTCTCTTTCTG  
 TTTTATCTGACAGATTGAACGAGAGAGACTGCCTTGAACCTGATTATGTTTGCGGC  
 5 ATACCGTTTGTGTTCAACGGGCTATGCTGCAGTGGAAATTTGTGTTTTATCTGCATAG  
 CCCAAAAGTATTAACGCGGTGATGTCTTCTATTCCCATCTAGTAGTAGTAGGCGG  
 CCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCATGCGACGTCATAGCTCTTCTAT  
 AGTGTCACCTAAATTCAATTCAGTGGCCGTCGTTTTACAACGTCGTGACTGGGAAAA  
 CCCTGGCGTTACCCAACCTTAATCGCCTTGCAGCACATCCCCCTTTCGCCAGCTGGCG  
 10 TAATAGCCGAAGAGGCCCGCACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGAAT  
 GGCGAATGGGG (SEQ ID NO:236)

**Translation:**

15 LNERDCLEPDYVCGIPFVFNGLCCSGICVFICIAQKY (SEQ ID NO:237)

**Toxin Sequence:**

20 Asp-Cys-Leu-Xaa1-Xaa3-Asp-Xaa5-Val-Cys-Gly-Ile-Xaa3-Phe-Val-Phe-Asn-Gly-Leu-Cys-  
 Cys-Ser-Gly-Ile-Cys-Val-Phe-Ile-Cys-Ile-Ala-Gln-Lys-Xaa5-^ (SEQ ID NO:238)

**Name:** Marm14  
**Species:** marmoreus  
 25 **Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

30 GGTACGCCTGCAGGTACCGGTCCGGAATTCCCGGGTCGACATCATCATCATCGA  
 TCCATCTGTCCATCCATCTATTCATTCATTCGCTGTCAAACCTGTAATACATATTAGAA  
 TCTCTCTTTCTGTTTGTATCTGACAGATTGGAGAAAAGGGCGTGCAGCAAAAAATGG  
 GAATATTGTATAGTACCGATCCTTGGATTCTGATATTGCTGCCCTGGCTTAATCTGTG  
 GTCCTTTCGTCTGCGTTTGATAGTGATGTCTTCTCTCCCATCTAGTAGTAGTAGGCG  
 35 GCCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCATGCGACGTCATAGCTCTTCTA  
 TAGTGTCACCTAAATTCAATTCAGTGGCCGTCGTTTTACAACGTCGTGACTGGGAAA  
 ACCCTGGCGTTACCCAACCTTAATCGCCTTGCAGCACATCCCCCTTTCGCCAGCTGGC  
 GTAATAAGCGAAGAGGCCCGCACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGAA  
 TGCGGAAATGGGACGCGCCCTG (SEQ ID NO:239)

**Translation:**

LEKRACSKKWEYCIVPILGFVYCCPGLICGPFVCV (SEQ ID NO:240)

15 **Toxin Sequence:**

Ala-Cys-Ser-Lys-Lys-Xaa4-Xaa1-Xaa5-Cys-Ile-Val-Xaa3-Ile-Leu-Gly-Phe-Val-Xaa5-Cys-Cys-

Xaa3-Gly-Leu-Ile-Cys-Gly-Xaa3-Phe-Val-Cys-Val-^ (SEQ ID NO:241)

**Name:** Omarial4  
**Species:** omaria  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

10 AAAGCCGGTACGCCTGCAGGTACCGGTCCGGAATTCCCGGGTCGACATCATCATCA  
 TCATCGATCCATCTGTCCATCCATCCATTCAATTCATTCCTGACAACTGTCATAAAT  
 ATTTGAGTCTCTCTTTCTGTTTTTATCTGACAGATTGAACGAGAGAGACTGCCTTAAT  
 GTTGATTATTTTTGTGGCATAACCGTTTGTGAACAACGGGCTATGCTGCAGTGGCAAT  
 15 TGTGTTTTTTGTCTGCACACCCCAAGGGAAGTAAACTGCCGTGATGTCTTCTCTTCC  
 CCTCTAGTAGTAGTAGGCGGCCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCAT  
 GCGACGTCATAGCTCTTCTATAGTGTACCTAAATTCAATTCCTGGCCGTCGTTTTA  
 CAACGTCGTGACTGGGAAAACCTGGCGTTACCCAACCTAATCGCCTTGCAGCACAT  
 CCCCCTTTCGCCAGCTGGCGTAATAGCGAAGAGGCCCGCACCGATCGCCCTTCCCA  
 20 ACAGTTGCGCAGCCTGAATGGCGAATGGGACGCGCCCT (SEQ ID NO:242)

**Translation:**

LNERDCLNVDYFCGIPFVNNGLCSSGNCVFCLHTPREVKLP (SEQ ID NO:243)

**Toxin Sequence:**

Asp-Cys-Leu-Asn-Val-Asp-Xaa5-Phe-Cys-Gly-Ile-Xaa3-Phe-Val-Asn-Asn-Gly-Leu-Cys-Cys-  
 Ser-Gly-Asn-Cys-Val-Phe-Cys-Leu-His-Thr-Xaa3-Arg-Xaa1-Val-Lys-Leu-Xaa3-^ (SEQ ID  
 30 NO:244)

**Name:** O6.4  
**Species:** obscurus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

10 cgatecatetgtccatccatccattcattcattcattgccaaaactgaacaaatattcaagtctctctttctgtttgtgtctgacagATCGAAA  
 CGGTGCCTTGTTTACGGTACACCTTGTGACTGGCTGACCATTGCGGGTATGGAGTGC  
 TGCAGTAAAAAGTGCTTTATGATGTGCTGGTAAACTGCCGTGATGTCTTCTACTCC  
 CCTC (SEQ ID NO:245)

**Translation:**

RSKRCLVYGTPCDWLTIAGMECCSKKCFMMCW (SEQ ID NO:246)

**Toxin Sequence:**

5 Cys-Leu-Val-Xaa5-Gly-Thr-Xaa3-Cys-Asp-Xaa4-Leu-Thr-Ile-Ala-Gly-Met-Xaa1-Cys-Cys-Ser-  
Lys-Lys-Cys-Phe-Met-Met-Cys-Xaa4-^ (SEQ ID NO:247)

**Name:** R6.4  
**Species:** radiatus  
 10 **Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

15 ATTGAACCAGAGAGACTGCCATGAAGTTGGTGAATTTTGTGGCTTACCGTTAATAAA  
 GAACGGGGCTATGCTGCAGTCAGATTTGTTTAGGTGTCTGCGCAAAAGTGTTTAAAA  
 CTGCCGTGATGTCTTCTACTCCCAT (SEQ ID NO:248)

**Translation:**

20 LNQRDCHEVGEFCGLPLIKNGLCCSQICLGVC AKVF (SEQ ID NO:249)

**Toxin Sequence:**

25 Asp-Cys-His-Xaa1-Val-Gly-Xaa1-Phe-Cys-Gly-Leu-Xaa3-Leu-Ile-Lys-Asn-Gly-Leu-Cys-Cys-  
 Ser-Gln-Ile-Cys-Leu-Gly-Val-Cys-Ala-Lys-Val-Phe-^ (SEQ ID NO:250)

**Name:** R6.6  
 30 **Species:** radiatus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

35 ATTAGACAAGAAAGAGTGC ACTGCCAATGGTGAATTTTGTGGCATATCGGTCTTTGG  
 AAGCTACCTATGCTGCAGTGGCCGGTGTGTATTTCGTCTGCATCTAGTTGAACTGCCG  
 TGATGTCTTCTACTCCCCT (SEQ ID NO:251)

**Translation:**

40 LDKKECTANGEFCGISVFGSYLCCSGRCVFVCI (SEQ ID NO:252)

**Toxin Sequence:**

45 Xaa1-Cys-Thr-Ala-Asn-Gly-Xaa1-Phe-Cys-Gly-Ile-Ser-Val-Phe-Gly-Ser-Xaa5-Leu-Cys-Cys-  
 Ser-Gly-Arg-Cys-Val-Phe-Val-Cys-Ile-^ (SEQ ID NO:253)

**Name:** R6.7  
**Species:** radiatus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

10 ATTGGACAAGAAAGAGTGCACCTACCAATGGTGAATTTTGTGGCATATCGGTCTTTGC  
AAGCTTCCTATGCTGCAGTGGCCTGTGTGTATTCGTCTGCATCTAGCTGAACTGCCG  
TGATGTCTTCTCTTCCCCT (SEQ ID NO:254)

**Translation:**

15 LDKKECTTNGEFCGISVFASFLCCSGLCVFVCI (SEQ ID NO:255)

**Toxin Sequence:**

20 Xaa1-Cys-Thr-Thr-Asn-Gly-Xaa1-Phe-Cys-Gly-Ile-Ser-Val-Phe-Ala-Ser-Phe-Leu-Cys-Cys-  
Ser-Gly-Leu-Cys-Val-Phe-Val-Cys-Ile-^ (SEQ ID NO:256)

**Name:** R6.8  
**Species:** radiatus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

30 ATTGGACAAGAGAAAAATGCTTTCCCAAAAATCATTTTTGTGGCTTTGTGGTGATGCT  
GAACTACCTATGCTGCAGTGGCCGGTGTATATTCGTCTGCGTCTAGTTGAACTGCCG  
TGATGTCTTCTACTCCCAT (SEQ ID NO:257)

**Translation:**

35 LDKRKCFPKNHFCGFVVMLNYLCCSGRCIFVCV (SEQ ID NO:258)

**Toxin Sequence:**

40 Lys-Cys-Phe-Xaa3-Lys-Asn-His-Phe-Cys-Gly-Phe-Val-Val-Met-Leu-Asn-Xaa5-Leu-Cys-Cys-  
Ser-Gly-Arg-Cys-Ile-Phe-Val-Cys-Val-^ (SEQ ID NO:259)

45 **Name:** Rg6.5  
**Species:** regius  
**Isolated:** No



**Cloned:** Yes

**DNA Sequence:**

5 TTGAACAAGAGAAGCTGCCTTCCTCTAGACTGGTTTTGTGGCTTCAATATAATTGGA  
GCGTTTCTGTGCTGTAGTGGCTACTGCCTTGTCGTCTGCATGTAAACTGCCGTGAT  
GTCTTCTCCTCCCCTC (SEQ ID NO:260)

**Translation:**

10 LNKRSCLPLDWFCGFNIIGAFLCCSGYCLVVCM (SEQ ID NO:261)

**Toxin Sequence:**

15 Ser-Cys-Leu-Xaa3-Leu-Asp-Xaa4-Phe-Cys-Gly-Phe-Asn-Ile-Ile-Gly-Ala-Phe-Leu-Cys-Cys-  
Ser-Gly-Xaa5-Cys-Leu-Val-Val-Cys-Met-^ (SEQ ID NO:262)

**Name:** De6.2

20 **Species:** delessertii

**Isolated:** No

**Cloned:** Yes

**DNA Sequence:**

25 ATGAAACTGACGTGTCTGCTGATCGTTGCTGTGCTGGTCTTGGCAGCCTGTCAGTTC  
ATCGTAGCTGGCGACTCGAGTGATGGCCAGGAGAATCCTGCTCTGAGGTCACCTAG  
CGATTCTCTGGGAAAATGTCATCAATGAAGCGCTTCCAGACACGGCTGATGGTGG  
GGCAATCTGCATCGAAAAGACCAAGCAAGAGGGACTGCATCCCCGGCGGCGAAAA  
30 TTGTGATGTATTCCGACCATAACCGGTGCTGCAGTGGATATTGCATACTACTCCTTTG  
CGCATGATAAAGCTGCCTTGATGTCTTCTCCTCCCCTC (SEQ ID NO:263)

**Translation:**

35 MKLTCLLIVAVLVLAACQFIVAGDSSDGQENPALRSPSDSSGKMSSMKRFQTRLMVGGQ  
SASKRPSKRDCIPGGENCDFRPPYRCCSGYCILLCA (SEQ ID NO:264)

**Toxin Sequence:**

10 Asp-Cys-Ile-Xaa3-Gly-Gly-Xaa1-Asn-Cys-Asp-Val-Phe-Arg-Xaa3-Xaa5-Arg-Cys-Cys-Ser-  
Gly-Xaa5-Cys-Ile-Leu-Leu-Leu-Cys-Ala-^ (SEQ ID NO:265)

**Name:** Striat21

15 **Species:** striatus

**Isolated:** No

**Cloned:** Yes

**DNA Sequence:**

5 GCTGGTTCGCCTGCAGGTACCGGTCCGGAATTCCCGGGTTCGACATCATCATCATCGA  
 TCCATCTGTCCATCCATCTATTCAATTCATTCATTCGCTGCCAACTGTATTAAATATT  
 CAAGTCTCTCTTTCTGTTTGTGTCTAACAGATTGAGATGGTGCATTCCTAGTGGTGA  
 ACTTTGTTTCCGCTCGGATCACATAGGATGCTGCAGTGGCAAGTGCGCATTCGTCTG  
 CTTGTAAAACTGCCGTGATGTCTTCTCCTCCCATCTAGTAGTAGTAGGCGGCCGCTC  
 TAGAGGATCCAAGCTTACGTACGCGTGCATGCGACGTCATAGCTCTTCTATAGTGTC  
 10 ACCTAAATTCAATTCAGTGGCCGTCGTTTTACAACGTCGTGACTGGGAAAACCTGG  
 CGTTACCCAACCTTAATCGCCTTGCAGCACATCCCCCTTTCGCCAGCTGGCGTAATAG  
 CGAAGAGGCCCGCACCCGATCGCCCTTCCCAACAGTTTGCGCAGCCTGAATGGCGAA  
 TGGGACGCGCCCTGTAGCGGCGCATTAACCGCGGCGGGTGTGGGTGGGTACGCC  
 CACGTGACCCGCTACACTTGCCAGCGCCCTANCGCCCCGCTCCTTTCGCTTTCTTTCC  
 15 CTTCTTTCTCGNCACGTTTCGGCCGNTTTTCCCCGTCAAGCTCTTAAATCGGGGGG  
 CTTCCCTTTAAGGGTTNCCGAATTANTGCTTTACCGGNACCCTTGACCCCCAAAAAA  
 ACTTGGANTAAGGGGNGATGGNTCNCGTAANTGGGGGCCATCNCCTGAANAGA  
 ACGGTTTTTCNCCCCTTTTGACNGTTGGGNGTTCCNCGGTTTTTAAAAAANGGGACC  
 TTTTNTTCCAAAACCTGGGAANANACCTAAACCCTATTTTGGGGCTATTTTTTTGAN  
 20 TTTNAAANGGGATTTTGCCCCATTTTNGGCCCTNTTGGGGTAAAAAAAAGAGCCGG  
 TTTTAAAAAAATTTTACCCCAAATTTTAACAAAAATTTTTT (SEQ ID NO:266)

**Translation:**

25 LRWCIPSGELCFRSDHIGCCSGKCAFVCL (SEQ ID NO:267)

**Toxin Sequence:**

30 Leu-Arg-Xaa4-Cys-Ile-Xaa3-Ser-Gly-Xaa1-Leu-Cys-Phe-Arg-Ser-Asp-His-Ile-Gly-Cys-Cys-  
 Ser-Gly-Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:268)

**Name:**  $\delta$ Striatus 26

**Species:** striatus

35 **Isolated:** No

**Cloned:** Yes

**DNA Sequence:**

10 TTGAGATGGTGCATTCCTAGTGGTGATCTTTGTTTCCGCTCGGATCACATAGGATGC  
 TGCAGTGGCAAGTGCGCATTCGTCTGCTTGTA (SEQ ID NO:269)

**Translation:**

15 LRWCIPSGDLCFRSDHIGCCSGKCAFVCL (SEQ ID NO:270)

**Toxin Sequence:**

Xaa4-Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Arg-Ser-Asp-His-Ile-Gly-Cys-Cys-Ser-Gly-Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:271)

5

**Name:**  $\delta$ Striatus 106  
**Species:** striatus  
**Isolated:** No  
**Cloned:** Yes

10

**DNA Sequence:**

TTGAGATGGTGCATTCCTAGTGGTGATCTTTGTTTCCGCTCGGATCACATACAATGC  
 TGCAGTGGCAAGTGCGCATTCGTCTGCTTGTA (SEQ ID NO:272)

15

**Translation:**

LRWCIPSGDLCFRSDHIQCCSGKCAFVCL (SEQ ID NO:273)

20

**Toxin Sequence:**

Xaa4-Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Arg-Ser-Asp-His-Ile-Gln-Cys-Cys-Ser-Gly-Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:274)

25

**Name:** O6.3  
**Species:** obscurus  
**Isolated:** No  
**Cloned:** Yes

30

**DNA Sequence:**

cgatccatctgtccatccatccattcagtcattcgtgcgcaactgtaacaaatattcaagtcttgccttctgtttgtgtctgacagATTGAG  
 ATGGTGC GTTCCTAGCGGTGAAGTTTGTCTGCCGCTATGAATTCGTGGGATGCTGCAG  
 TGGCAAGTGCTTCTTCGTCTGCTCGTAAACTGTTGTGATGTCTTCTCCTCCCCCTC  
 (SEQ ID NO:275)

35

**Translation:**

10 VSDRLRWCVPSPGEVCRRYEFVGCCSGKCFVCS (SEQ ID NO:276)

**Toxin Sequence:**

Leu-Arg-Xaa4-Cys-Val-Xaa3-Ser-Gly-Xaa1-Val-Cys-Arg-Arg-Xaa5-Xaa1-Phe-Val-Gly-Cys-Cys-Ser-Gly-Lys-Cys-Phe-Phe-Val-Cys-Ser-^ (SEQ ID NO:277)

15

**Name:** R6.3  
**Species:** radiatus  
**Isolated:** No  
**Cloned:** Yes

5

**DNA Sequence:**

ctctctctctctgctggacaggTCGACTCGCTGCTTGCCTGACGGAACGTCTTGCCTTTTTAGTA  
GGATCAGATGCTGCGGTACTTGCAGTTCAATCTTAAAGTCATGTGTGAGCTGATCCG  
10 GCGGTTGATCTTCCTCCCTCTGTGCTCCATCCTTTTCTGCCTGAGTCCTCCTTACCTG  
AGAGTGGTCATGAACCACTCATCACCTACTCCTCTGGAGGCTTCAGAGGAGCTACAT  
TGAAATAAAAGCCGCATTGC (SEQ ID NO:278)

**Translation:**

15

RSTRCLPDGTSCFLSRIRCCGTCSSILKSCVS (SEQ ID NO:279)

**Toxin Sequence:**

20 Cys-Leu-Xaa3-Asp-Gly-Thr-Ser-Cys-Leu-Phe-Ser-Arg-Ile-Arg-Cys-Cys-Gly-Thr-Cys-Ser-Ser-  
Ile-Leu-Lys-Ser-Cys-Val-Ser-^ (SEQ ID NO:280)

**Name:** G6.3  
**Species:** geographus  
25 **Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

30 GGATCTTGCACGGTGAATTTTCGCTTCATATTTTCTACTGTCGTCTTTGGCATCATCC  
AAAACATCACCAAGATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGA  
CCGCCTGGACATTCGTCACGGCTGTGCCTCACTCCAGCGATGTATTGGAGAATCTTT  
ATCTGAAGGCACTTCACGAAACGGAAAACACGAAGCCTCTAAATTGAACGTGAGA  
GACGACGAGTGCGAACCTCCTGGAGATTTTTGTGGCTTTTTTAAATTTGGGCCGCT  
35 TGCTGCAGTGGCTGGTGCTTCCTCTGGTGCGCCTAAAACCTGCCGTGATGTCTTCTATT  
CCCCTCTGTGCTACCTGGCTTGATCTTTGATTGGCGCGTGCCCTTCAGTGGTTATGAA  
CCCCCTGAGCCGACTCTCTGGGGGCTCGGGGGTTCAACATCCAAATAAAGCGAC  
AACACAATCACAAGTAAAAAA (SEQ ID NO:281)

10 **Translation:**

MKLTCMMIVAVLFLTAWTFVTAVPHSSDVLENLYLKALHETENHEASKLNVRDDECEP  
PGDFCGFFKIGPPCCSGWCFLWCA (SEQ ID NO:282)

15 **Toxin Sequence:**

Asp-Asp-Xaa1-Cys-Xaa1-Xaa3-Xaa3-Gly-Asp-Phe-Cys-Gly-Phe-Phe-Lys-Ile-Gly-Xaa3-Xaa3-

Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Leu-Xaa4-Cys-Ala-<sup>^</sup> (SEQ ID NO:283)

**Name:** Tx6.8  
**Species:** textile  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

GCTGCAGGTCGACTCTAGAGGCGTTGGAGAATCTTTATCTGAAGGCACATCATGAA  
 ATGAACAACCCCGAAGACTCTGAATTGAACAAGAGGTGCTATGATAGTGGGACAAG  
 TTGTAACACTGGAAACCAATGCTGCAGTGGCTGGTGCATTTTCGTCTGCCTCTAAAA  
 CTGCCGTGATGTCTTCTACTCCCCTCTGTGCTACCTACCTGGCTTGATCTTTGATTGG  
 CGCGTGCCCTTCACTGGTTATGAACCCCTCTGATCCGACTCTCTGGGGGGCCTCGGGG  
 ATCCAACATCAAAATANAGCGACAGCACAATCAC (SEQ ID NO:284)

**Translation:**

CRSTLEALENLYLKAHHEMNNPEDSELNKRCDYSGTSCNTGNQCCSGWCIFVCL (SEQ ID NO:285)

**Toxin Sequence:**

Cys-Xaa5-Asp-Ser-Gly-Thr-Ser-Cys-Asn-Thr-Gly-Asn-Gln-Cys-Cys-Ser-Gly-Xaa4-Cys-Ile-Phe-Val-Cys-Leu-<sup>^</sup> (SEQ ID NO:286)

-----

**Name:** Qc6.1  
**Species:** quercinus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

GCTTCGTATTTCTCCGCTGTCTTCCTTGGCATCACCCAAAACATCACCAAGATGAAA  
 CTGACGTGCATGATGATCGTTGCTCTGCTGTTCTTGACCGCCTGGACATTCGTCACG  
 GCTGTTGACTCCAAAAATGAACTGGAGaACAGAGGAGGATGGGGGCAGGCAGGAG  
 GATGGGGGAAACTTTTTCCGATGGCACGCGACGAAATGAAAAACAGCGAAGTCTCT  
 AAATTGGACAATAAGAGAAAAGTGCCTGACGCCGTGAAGCTTGCGTAAACCTAT  
 CATTGGaAACGTATTTTGCTGCAAAGGCTACTGtCTTTTCGTCTGCATTAGTTAACT  
 GcTGTGATGCcTTCTACTCACCTCTGTGCTACCTGGCTTGATCTTTGATTGGCGTGTGC  
 CCTTCACTGGTTATGAgCTCGTCTGAcCTACTCTCTGGAGACCTCTGTGGTCCAACA  
 CCaAATAAAGCGGcATCCCAATc (SEQ ID NO:287)

**Translation:**

MKLTTCMMIVALLFLTAWTFVTAVDSKNELENRGGWGQAGGWGKLFPMARDEMKNSE  
VSKLDNKRKCAAAGEACVIPIIGNVFCCKGYCLFVCIS (SEQ ID NO:288)

5 **Toxin Sequence:**

Cys-Ala-Ala-Ala-Gly-Xaa1-Ala-Cys-Val-Ile-Xaa3-Ile-Ile-Gly-Asn-Val-Phe-Cys-Cys-Lys-Gly-  
Xaa5-Cys-Leu-Phe-Val-Cys-Ile-Ser-^ (SEQ ID NO:289)

10 -----

**Name:** Lp6.5  
**Species:** leopardus  
**Isolated:** No  
15 **Cloned:** Yes

**DNA Sequence:**

20 ATGAAACTGACGTGCGTGGTGATCGTTGCTGTGCTGTTCTTGACCGCCTGGATATTC  
ATCACGGCTGATGACTCCACAAATGGACTGGAGAATCGTTTTAGGAAGGCACGTGA  
CAACATGAAGAACGCCAAAGCCTCTACATTAGCCGAGAAGAAAGCGTGTGTTGAAC  
TTGGTGAGATTTGTGCCACAGGCTTCTTCCTAGACGAGGAATGCTGCACTGGTTCAT  
GCCATGTCTTCTGCGTACTATAGTTAAACTGCTGTGATGTCTTCTTCTCCTCCGTG  
25 CTACCTGGCTTGATCTTTGATTGGTGCCTGTCCTTCAGTGGTTGTGAAACCCTCTGAT  
CCTACTCTCTGGACGCCTCTGAGGCCCAACATCCAAATAAAGCGACATCCTAATGCC  
AAAAAAAAAAAA (SEQ ID NO:290)

**Translation:**

30 MKLTCVVIVAVLFLTAWIFITADDSTNGLENRFRKARDNMKNKASTLAIEKKACVELG  
EICATGFFLDEECCTGSCHVFCVL (SEQ ID NO:291)

**Toxin Sequence:**

35 Ala-Cys-Val-Xaa1-Leu-Gly-Xaa1-Ile-Cys-Ala-Thr-Gly-Phe-Phe-Leu-Asp-Xaa1-Xaa1-Cys-Cys-  
Thr-Gly-Ser-Cys-His-Val-Phe-Cys-Val-Leu-^ (SEQ ID NO:292)

-----

10 **Name:** Mr6.4  
**Species:** marmoreus  
**Isolated:** No  
15 **Cloned:** Yes

15 **DNA Sequence:**

ATGAAACTGACGTGCGTGGTGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTT

GCCACGGCTGATGACCCCAGAAATGGATTGGAGAATCTTTTTTCGAAGGCACATCA  
 CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCCCTAACACTGGTG  
 AATTATGTGATGTGGTTGAACAAAAGTCTGCTATACCTATTGCTTTATTGTAGTCT  
 GCCTATAAAACTACCGTGATGTCTTCTACTCCCCCTCTGTGCTGCCTGGCTTGATCTTT  
 5 GATTGGCGCGTGCCCTTCACTGGTTATGACCCCCCTGATCCGACCTCTGGGG (SEQ  
 ID NO:293)

**Translation:**

10 MKLTCVVIVAVLFLTAWTFATADDPRNGLENLFSKAHHEMKNPEASKLNKRCNPNTGEL  
 CDVVEQNCCYTYCFIVVCL (SEQ ID NO:294)

**Toxin Sequence:**

15 Cys-Xaa3-Asn-Thr-Gly-Xaa1-Leu-Cys-Asp-Val-Val-Xaa1-Gln-Asn-Cys-Cys-Xaa5-Thr-Xaa5-  
 Cys-Phe-Ile-Val-Val-Cys-Leu-^ (SEQ ID NO:295)

-----  
 20 **Name:** Qc6.2  
**Species:** quercinus  
**Isolated:** No  
**Cloned:** Yes

25 **DNA Sequence:**

GGATCCATGAAACTGACGTGTATGGTGATCGTTGCTGTGCTATTCTTGACCGCCTCG  
 GCTGATGACTCCAGAAATGGATTTCGAGAATCGAAATGGAGAACGAAACGAAAACG  
 AAATGAAGAACCTCGAAGCCTCTAAATTGAACAGGAGAGACGGCGATTGCGTTGAT  
 30 GGTGGTGAATTTTGTGGCTTTCCGAAAATTGGAGGGCCATGCTGTAGTGGCTGGTGC  
 TTTTTCGTCTGCTTATAAAACTGCCATGATGTCTTCTACCCCCCTCTGTGCTACCTGA  
 CTTGATCTTTGATTGGCGTGTGCCCTTCACTGGTTATGAACCCCTCTGATCCGACTCT  
 CTGGAGGCCTCGGGGGTCCAACATCCAAATAAAGCGACAGCAAAAAAAAAAAAAAA  
 AAAAAA (SEQ ID NO:296)

35 **Translation:**

MKLTCMVIVAVLFLTASADDSRNGFENRNGERNENEMKNLEASKLNRRDGDGDCVDGGE  
 FCGFPKIGGPCCSGWCFFVCL (SEQ ID NO:297)

40 **Toxin Sequence:**

Asp-Gly-Asp-Cys-Val-Asp-Gly-Gly-Xaa1-Phe-Cys-Gly-Phe-Xaa3-Lys-Ile-Gly-Gly-Xaa3-Cys-  
 Cys-Ser-Gly-Xaa4-Cys-Phe-Phe-Val-Cys-Leu-^ (SEQ ID NO:298)

45  
 -----

**Name:** Qc6.3  
**Species:** quercinus  
**Isolated:** No  
**Cloned:** Yes

5

**DNA Sequence:**

GGATCCATGAAACTGACGTGCGTGGTGATCGTTGCTGTGCTATTCTTGACCGCCTTG  
 GCTGATGACTCCAGAAATGGATTGGAGAATCGAAATGAACAAGAACGAAACGAAA  
 10 ACGAAATGAGGGACCGCCGGGACTGCCAAGATAGTGGTGTAGTTTGTGGCTTTCCG  
 AAACCTGAACCACACTGCTGCAGTGGCTGGTGCCTTTTCGTCTGCGCCTAAACTGC  
 CGTGATGTCAAATAAAGCGACAGACAATNAAAAAAAAAAAAAAAAAAAAA (SEQ ID  
 NO:299)

1.5 **Translation:**

MKLTCVVIVAVLFLTALADDSRNGLENRNEQERNENEMRDRRDCQDSGVVCGFPKPEP  
 HCCSGWCLFVCA (SEQ ID NO:300)

20 **Toxin Sequence:**

Asp-Cys-Gln-Asp-Ser-Gly-Val-Val-Cys-Gly-Phe-Xaa3-Lys-Xaa3-Xaa1-Xaa3-His-Cys-Cys-  
 Ser-Gly-Xaa4-Cys-Leu-Phe-Val-Cys-Ala-^ (SEQ ID NO:301)

2.5 -----

**Name:** Ar6.5  
**Species:** arenatus  
**Isolated:** No  
 30 **Cloned:** Yes

**DNA Sequence:**

GGATCCATGAAACTGACGTGTGTGGTGATCGTTGCTGTGCTGTTCTTGACCGCCTGG  
 3.5 ACATTCGTACGGCTGACTCCATACGTGCACTGGAGGATTTTTTTGCGAAGGCACGT  
 GACGAAATGGAACAGCGGAGCTTCTCCATTGAACGAGAGAGACTGCCGACCTGT  
 AGGTCAATATTGTGGCATAACCGTATAAGCACAACTGGCGATGCTGCAGTCAGCTTTC  
 TGCAATTATCTGTGTTTCCTAACCCCTCTGATCCTACTCTCTGAAGACCTCCGGGATT  
 CAACATCCAAATAAAGCGACATCCCGATNAAAAAAAAANGAAAAAAAAAAAAAAAAA  
 10 (SEQ ID NO:302)

**Translation:**

MKLTCVVIVAVLFLTAWTFVTADSIRALEDFFAKARDEMENS GASPLNERDCRPVGQY  
 1.5 CGIPYKHNWRCCSQLCAIICVS (SEQ ID NO:303)

**Toxin Sequence:**



Asp-Cys-Arg-Xaa3-Val-Gly-Gln-Xaa5-Cys-Gly-Ile-Xaa3-Xaa5-Lys-His-Asn-Xaa4-Arg-Cys-  
Cys-Ser-Gln-Leu-Cys-Ala-Ile-Ile-Cys-Val-Ser-^ (SEQ ID NO:304)

5 -----

**Name:** Ar6.11  
**Species:** arenatus  
**Isolated:** No  
10 **Cloned:** Yes

**DNA Sequence:**

15 GGATCCATGAAACTGACGTGTGTGGTGATCGTTGTTGTGCTGTTCTTGACCGCCTGG  
ACATTCGTCAAGGCTGATGACTCCATAAATGGATTGGAGAATCTTTTCCGAAGGCA  
CGTCACGAAATGAAGAACCCCGAAGCCTCTAAATTGAACGAGAGGTGCCTTGAAAA  
GGGTGTACTTTGTGATCCGAGTGCTGGAAACTGCTGTAGTGGCGAATGCGTTTTAGT  
CTGCCTCTAAAACTACCGTGATGTCTTCTACTCCCATCTGTGCTACCCCTCGAG (SEQ  
ID NO:305)

20

**Translation:**

MKLTCVVIVVVLFLTAWTFVKADDSINGLENLFPKARHEMKNPEASKLNERCLEKGVL  
CDPSAGNCCSGECVLVCL (SEQ ID NO:306)

25

**Toxin Sequence:**

Cys-Leu-Xaa1-Lys-Gly-Val-Leu-Cys-Asp-Xaa3-Ser-Ala-Gly-Asn-Cys-Cys-Ser-Gly-Xaa1-Cys-  
Val-Leu-Val-Cys-Leu-^ (SEQ ID NO:307)

30

-----

**Name:** Ar6.12  
**Species:** arenatus  
35 **Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

10 GGATCCATGAAACTGACGTGCATGGTGATCGTTACTGTGTTGTTCTTGACCGCCTGG  
ACATTCGTACGGCTGATGACTCCAGAAATGAATTGGAGAATCTTTTCTGAAGGCA  
TATCACGAAATGAACTCCGAAGCCTCTAAATTGGACAAGAAAGAGTGCCTTGCTGG  
TAGTCACTTTTGTGGTTTTCCGAAAATTGGAGGGCCATGCTGCAGTGGCTGGTGCTT  
TTTCGTCTGCTTGTAACCTGCCGTGATGTCTTCTACTCCCATCTGTGCTACCCCTCG  
15 AG (SEQ ID NO:308)

**Translation:**

MKLTCMVIVTVLFLTAWTFVTADDSRNELENFLKAYHEMNSEASKLDKKECVAGSHF  
CGFPKIGGPCCSGWCFFVCL (SEQ ID NO:309)

5 **Toxin Sequence:**

Xaa1-Cys-Val-Ala-Gly-Ser-His-Phe-Cys-Gly-Phe-Xaa3-Lys-Ile-Gly-Gly-Xaa3-Cys-Cys-Ser-  
Gly-Xaa4-Cys-Phe-Phe-Val-Cys-Leu-^ (SEQ ID NO:310)

10 -----

**Name:** Ts6.2  
**Species:** tessulatus  
**Isolated:** No  
15 **Cloned:** Yes

**DNA Sequence:**

GGATCCATGAAACTGACGTGTGTGGTGATCGTTGCTGTGATGTTCTTGACCGCCTGG  
20 ACATTCATCACGGCTGATGACTCCATAAATGGACTGGAGGATAGAGGCATATGGGG  
GGAACCTTTGTCTGAAGGCACGTGACGAAATGAACCCCGAAGTCTCTAAACGGGATT  
GCTGGCCTCAATATTGGTTTTGTGGCCTACAGAGGGGATGCTGCCCAGGGACTACTT  
GCTTCTTCCTTTGCTTTTAGTGATCTCTTCGACTCCCTTCTGTGCTACCTGGCTTGACC  
TTTGATTGGCGCGTGCCCTTCACTGGTTATAAACCCCTCTGTTCCCTCCTCTCTGGACG  
25 CTTTCGGGGTGTCCAGCATCCAAATAAAGCGACGTCCCCAAAAAAAAAAAAAAAAAAAA  
AA (SEQ ID NO:311)

**Translation:**

30 MKLTCVVIVAVMFLTAWTFITADDSINGLED RGIWGEPLSKARDEMNP EVSKRDCWPQ  
YWFCGLQRGCCPGTTCFFLCF (SEQ ID NO:312)

**Toxin Sequence:**

35 Asp-Cys-Xaa4-Xaa3-Gln-Xaa5-Xaa4-Phe-Cys-Gly-Leu-Gln-Arg-Gly-Cys-Cys-Xaa3-Gly-Thr-  
Thr-Cys-Phe-Phe-Leu-Cys-Phe-^ (SEQ ID NO:313)

-----

10 **Name:** Ts6.4  
**Species:** tessulatus  
**Isolated:** No  
**Cloned:** Yes

15 **DNA Sequence:**

GGATCCATGAAACTGACGTGCGTGGTGGTCGTTGCTGTGCTGTTCTTGAACGCCTGG

ACATTCGCCACGGCTGTTGACTCCAAACATGCACTGGCGAAACTTTTTATGAAGGCA  
 CGTGACGAAATGTATAACCCCGATGCCACTAAATTGGACGATAAGAGATGGTGCGC  
 TTTAGATGGTGAACCTTTGTATCATACCGGTCATTGGGTCCATATTTTGCTGCCATGGC  
 ATATGTATGATCTACTGCGTCTAGTTGAACTGCCGTGATGTCTTCTACTCCCCTCTGT  
 5 GCTACCCCTGGTTTGATCTTTGATTGCCCTGTGCCCTTCACTGATTATGAATCCCTCT  
 GATCCTACTCTCTGAAGACCTCTTGGGGTCCAACATCCAAATAAAGCGACATCCCAA  
 AAAAAAAAAAAAAAAAAA (SEQ ID NO:314)

#### Translation:

10 MKLTCVVVVAVLFLNAWTFATAVDSKHALAKLFMKARDEMYNPDATKLDDKRWCA  
 LDGELCHPVIGSIFCCHGICMIYCV (SEQ ID NO:315)

#### Toxin Sequence:

15 Xaa4-Cys-Ala-Leu-Asp-Gly-Xaa1-Leu-Cys-Ile-Ile-Xaa3-Val-Ile-Gly-Ser-Ile-Phe-Cys-Cys-His-  
 Gly-Ile-Cys-Met-Ile-Xaa5-Cys-Val-^ (SEQ ID NO:316)

-----

20 **Name:** Im6.1  
**Species:** imperialis  
**Isolated:** No  
**Cloned:** Yes

#### DNA Sequence:

GGATCCATGAAACTGACGTGCGTGGTGTTCGTTGCTGTGCCGTTCTTGACCGCCTCG  
 GTATTCATCACGGCTGATGACTCCAGAAATGGAATCGAGAATCTTCCTCGGATGAG  
 30 ACGTCACGAAATGAAGAACCCCAAAGCCTCTAAGTTGAACAAGAGACAGTGCCGTG  
 TAGAAGGTGAAATTTGTGGCATGCTGTTTGAAGCACAATGCTGCGATGGCTGGTGCT  
 TTTTCGTCTGCATGTAAAACTGCCGTGATGTCTTCTACTCTCCTCTGTGCTACCTGCC  
 CTGATCTTTGATTGGCTCGCGCCCTTCATTGGTTATGAACCCCTCTGATCCTACTCTC  
 TGGAGGCCTCAGGGGTCCAGCATCTAAATAAAGCGACATCACAAATCAAAAAAAAAA  
 35 AAAAAAAAAA (SEQ ID NO:317)

#### Translation:

10 MKLTCVVVFVAVPFLTASVFITADDSRNGIENLPRMRRHEMKNPKASKLNKRQCRVEGEI  
 CGMLFEAQCCDGCFFVCM (SEQ ID NO:318)

#### Toxin Sequence:

15 Xaa2-Cys-Arg-Val-Xaa1-Gly-Xaa1-Ile-Cys-Gly-Met-Leu-Phe-Xaa1-Ala-Gln-Cys-Cys-Asp-  
 Gly-Xaa4-Cys-Phe-Phe-Val-Cys-Met-^ (SEQ ID NO:319)

-----  
**Name:** Ca6.5  
**Species:** characteristicus  
5 **Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

10 GGATCCATGAAACTGACGTGTGTGGTGATCGTTGCTGTGCTGTTCTTGACCGCCTGG  
ACATTCGTCACGGCTGATGACTCCAGAAATGGATTGGAGAATCTTTTCCGAAGGCA  
CGTCACGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCGTTGACCC  
TGGTGAATTTTGTGGTCCGGGATTGAGATTGCTGCACTGGCTTCTGCCTTTTAGTC  
15 TGCATCTAAAACTGCCGTGATGTCTTCTACTCCCATCTGTGCTACCCCTCGAG (SEQ  
ID NO:320)

**Translation:**

20 MKLTCVVIVAVLFLTAWTFVTADDSRNGLENLFPKARHEMKNPEASKLNKRCVDPGEF  
CGPGFGDCCTGFCLLVCI (SEQ ID NO:321)

**Toxin Sequence:**

25 Cys-Val-Asp-Xaa3-Gly-Xaa1-Phe-Cys-Gly-Xaa3-Gly-Phe-Gly-Asp-Cys-Cys-Thr-Gly-Phe-Cys-  
Leu-Leu-Val-Cys-Ile-^ (SEQ ID NO:322)

-----  
30 **Name:** Mf6.2  
**Species:** miliaris  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

35 GGATCCATGAAACTGACGTGCGTGGTGATCGTTGCTGTGTTGTTCTTGACCGCCTGG  
ACATTCGTCATGGCTGATGACTCCAGAAATGATTTGGAGAATCTTTTCTGAAGGCA  
CGTCATGAAATGAAGAACCCCGAAGCTTCTAAATTGAACAAGAGATGCCTTCCAAA  
10 TGGTGTACTTTGTGATCTGGGATCTCCACCATACTGCTGCAGTGGCTGGTGCGCCAT  
CGTCGCTGTCATCTAAAACTGTCGTCATGTCTTCTACTCCCATCTGTGCTACCCCTCG  
AG (SEQ ID NO:323)

**Translation:**

15 MKLTCVVIVAVLFLTAWTFVMADDSRNDLENLFLKARHEMKNPEASKLNKRCLPNGV  
LCDLGSPPYCCSGWCAIVVCI (SEQ ID NO:324)

**Toxin Sequence:**

Cys-Leu-Xaa3-Asn-Gly-Val-Leu-Cys-Asp-Leu-Gly-Ser-Xaa3-Xaa3-Xaa5-Cys-Cys-Ser-Gly-Xaa4-Cys-Ala-Ile-Val-Val-Cys-Ile-<sup>^</sup> (SEQ ID NO:325)

5

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**Name:** Ak6.1  
**Species:** atlanticus  
**Isolated:** No  
**Cloned:** Yes

10

**DNA Sequence:**

15 GGATCCATGAAACTGACGTGCGTGGTGATCGTTGCTGTGCTGTTCTTGACCGCCTGG  
 ACATTCGTCACGGCTGATGACTCCATAAATGGGTTGGAGAATCTTTTCCGAAGGCA  
 CGTCACGAAATGAGGAAACCCGAAGCCTCTAGATCGAGAGGGAGGTGCCGTCCTCG  
 TGGTATGTTCTGTGGCTTTCCGAAACCTGGACCATACTGCTGCAATGGCTGGTGCTT  
 TTTCGTCTGCATCTAAAACTGCCGTGATGTGTTCTACTCCCATCTGTGCTACCCCTCG  
 20 AG (SEQ ID NO:326)

**Translation:**

25 MKLTCVVIVAVLFLTAWTFVTADDSINGLENLFPKARHEMRKPEASRSRGRCRPRGMF  
 CGFPKPGPYCCNGWCFFVCI (SEQ ID NO:327)

**Toxin Sequence:**

30 Cys-Arg-Xaa3-Arg-Gly-Met-Phe-Cys-Gly-Phe-Xaa3-Lys-Xaa3-Gly-Xaa3-Xaa5-Cys-Cys-Asn-  
 Gly-Xaa4-Cys-Phe-Phe-Val-Cys-Ile-<sup>^</sup> (SEQ ID NO:328)

-----

**Name:** Lv6.1  
**Species:** lividus  
**Isolated:** No  
**Cloned:** Yes

35

**DNA Sequence:**

10 GGATCCATGAAACTGACGTGCGTGGTGATCGTTGCTGTGCTGTTCTTGACCGCCTGG  
 ACATTTGCCACGGCTGATGACCCAGAAATGGATTGGAGAATCTTTTTCGAAGGCA  
 CATCACGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCCCTAACAC  
 TGGTGAATTATGTGATGTGGTTGAACAAAACCTGCTGCTATACCTATTGCTTTATTGT  
 15 AGTCTGCCTATAAACTACCGTCTATCTCTTCTACTCCCATCTGTGCTACCCCTCGAG  
 (SEQ ID NO:329)

**Translation:**

MKLTCVVIVAVLFLTAWTFATADDPRNGLENLFSKAHHHEMKNPEASKLNRCPNTGEL  
CDVVEQNCCYTYCFIVVCL (SEQ ID NO:330)

5

**Toxin Sequence:**

Cys-Xaa3-Asn-Thr-Gly-Xaa1-Leu-Cys-Asp-Val-Val-Xaa1-Gln-Asn-Cys-Cys-Xaa5-Thr-Xaa5-  
Cys-Phe-Ile-Val-Val-Cys-Leu-^ (SEQ ID NO:331)

10

-----  
**Name:** Pu6.3  
**Species:** pulicarius  
**Isolated:** No  
**Cloned:** Yes

15

**DNA Sequence:**

20 GGATCCATGAAACTGACGTGCATGGTGATCGTTGCTGTGCTGTTCTTGACCGCCTGG  
ACATTCGTCAAGGCTGATGACTCCAGAAATGGATTGGAGAATCTTTTTCCGAAGGC  
ACGTCACGAAATGAAGAACTCCAAAGCCTCTAAATTAAACAAGAGGTGCGTTGAAG  
ATGGTGATTTTTGTGGTCCGGGATATGAAGAGTGCTGCAGTGGCTTCTGCCTTTACG  
TCTGCATCTAAAAGTCCCGTGATGTCTTCTACTCCCATCTGTGCTACCCCTCGAG  
25 (SEQ ID NO:332)

**Translation:**

MKLTCMVIVAVLFLTAWTFVKADDSRNGLENLFPKARHEMKNKASKLNRKCVEDGD  
30 FCGPGYEECCSGFCLYVCI (SEQ ID NO:333)

**Toxin Sequence:**

Cys-Val-Xaa1-Asp-Gly-Asp-Phe-Cys-Gly-Xaa3-Gly-Xaa5-Xaa1-Xaa1-Cys-Cys-Ser-Gly-Phe-  
35 Cys-Leu-Xaa5-Val-Cys-Ile-^ (SEQ ID NO:334)

-----  
**Name:** Ge6.1  
**Species:** generalis  
**Isolated:** No  
**Cloned:** Yes

40

**DNA Sequence:**

45

GGATCCATGAAACTGACGTGTGTGGTGATCGTTGCTGTGCTATTCTTGACCGCCTGG  
ACATTCGTACGGCTGATGACACCAGATATAAACTGGAGAATCCTTTTCTGAAGGC

ACGCAACGAACTGCAGAAACACGAAGCCTCTCAACTGAACGAGAGAGGCTGCCTTG  
 ACCCAGGTTACTTCTGTGGGACGCCGTTTCTTGGAGCATACTGCTGCGGTGGCATT  
 GCCTTATTGTCTGCATAGAAACGTAAAGGCTTGATGTCTTCTACTCCCATCTGTGCT  
 ACCCCTCGAG (SEQ ID NO:335)

**Translation:**

MKLTCVVIVAVLFLTAWTFVTADDTRYKLENPFLKARNELQKHEASQLNERGCLDPGY  
 FCGTPFLGAYCCGGICLIVCIET (SEQ ID NO:336)

**Toxin Sequence:**

Gly-Cys-Leu-Asp-Xaa3-Gly-Xaa5-Phe-Cys-Gly-Thr-Xaa3-Phe-Leu-Gly-Ala-Xaa5-Cys-Cys-  
 Gly-Gly-Ile-Cys-Leu-Ile-Val-Cys-Ile-Xaa1-Thr-^ (SEQ ID NO:337)

-----  
**Name:** Ep6.1  
**Species:** episcopatus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

GGATCCATGAAACTGACGTGCGTGGTGATCGTTGCTGTGCTGTTCTTGACCGCCTGG  
 ACATTTGCCACGGCTGATGACCCCAAGAAATGGATTGGGGAATCTTTTTTCGAATGTA  
 CATCACGAAATGAAGAACCTCGAAGACTCTAAATTGGACAAGAAGTGCCTTGGGTT  
 TGGTGAAGCTTGTCTTATGCTTTATTCAGACTGCTGCAGCTATTGCGTTGCTCTTGTC  
 TGCCTATAAACTACCGTGACGTCTTCTACTCCCCTCTGTGCTACCTGGCTTGATCTT  
 TGATTGGCGTGTGCGCTTCACTGGTTATGAACCCCTCTGATCCTACTCTCTGAAGAC  
 CTCTGGGGTCCAACATCCAAATAAAGCGACATCACAAAAAAAAAAAAAAAAAAAAAA  
 AA (SEQ ID NO:338)

**Translation:**

MKLTCVVIVAVLFLTAWTFATADDPRNGLGNLFSNVHHEMKNLEDSKLDKKCLGFGE  
 ACLMLYSDCCSYCVALVCL (SEQ ID NO:339)

**Toxin Sequence:**

Cys-Leu-Gly-Phe-Gly-Xaa1-Ala-Cys-Leu-Met-Leu-Xaa5-Ser-Asp-Cys-Cys-Ser-Xaa5-Cys-Val-  
 Ala-Leu-Val-Cys-Leu-^ (SEQ ID NO:340)

-----  
**Name:** Ep6.2  
**Species:** episcopatus

**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

5 GGATCCATGAAACTGACGTGCGTGGTGATCATTGCTGTGCTGTTCTTGACCGCCTGG  
ACATTTCGTCATGGCTGATGACCCCAGAGATGAACCGGAGGCACGTGACGAAATGAA  
CCCCGCAGCCTCTAAATTGAACGAGAGAGGCTGCCTTGCA GTTGATTATTTTTCGCGG  
CATAACGTTTGTGAGCAACGGGCTATGCTGCAGTGGCAATTGTGTTTTTGTCTGCAC  
10 ACCCCAAGGGAAGTAAACTGCCGTGACGTCTTCTACTCCCCTCTGTGCTACCTGGC  
TTGATCTTTGATTGGCGTGTGCACTTCACTGGTTATGAACCCCTCTGATCCTACTCTC  
TGAAGACCTCTGGGGTCCAACATCCAAATAAAGCGACATCCCCAAAAAAAAAAAAAA  
AAAAAAA (SEQ ID NO:341)

**15 Translation:**

MKLTCVVIIAVLFLTAWTFVMADDPRDEPEARDEMNPAAASKLNERGCLAVDYFCGIPF  
VSNGLCCSGNCV FVCTPQGK (SEQ ID NO:342)

**20 Toxin Sequence:**

Gly-Cys-Leu-Ala-Val-Asp-Xaa5-Phe-Cys-Gly-Ile-Xaa3-Phe-Val-Ser-Asn-Gly-Leu-Cys-Cys-  
Ser-Gly-Asn-Cys-Val-Phe-Val-Cys-Thr-Xaa3-Gln-# (SEQ ID NO:343)

25 -----

**Name:** Ac6.1  
**Species:** achatinus  
**Isolated:** No  
30 **Cloned:** Yes

**DNA Sequence:**

3.5 CGATCCTCTGTCCTCCATCTATTATTATTCGCTGCCAAACTGTGTTAAATATTCAAGT  
CTCTCTTTCTGTTTGTGTCTAACAGGTTGAGATGGTGCATTCCTAGAGGTGATCTTTG  
TTTCCCCTCGGATCGCATACAATGCTGCAGTGGCAAGTGCACATTTCGTCTGCATGTA  
AAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:344)

**Translation:**

10 LRWCIPRGDLCFPSDRIQCCSGKCTFVCM (SEQ ID NO:345)

**Toxin Sequence:**

1.5 Xaa4-Cys-Ile-Xaa3-Arg-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-Arg-Ile-Gln-Cys-Cys-Ser-Gly-  
Lys-Cys-Thr-Phe-Val-Cys-Met-^ (SEQ ID NO:346)



-----

**Name:** Ac6.2  
**Species:** achatinus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

10 CGATCCTCTGTCCTCCTCCTTCATTCATTCGCTGCCAAACTGTATTAAATATTCTGAAT  
 CTCTCTTTCTGTTTGTGTCTGACAGATTGAGAGGGTGC GTTCCTAGTGGTGAAATTTG  
 TTA CTTCATGGATCACATAGGATGCTGCAGTGGCAAGTGCACATTTCGTCTGCATGTA  
 AAACTGCCGTGATGTCTTCTCCTCCCATC (SEQ ID NO:347)

**Translation:**

LRGCVPSGEICYFMDHIGCCSGKCTFVCM (SEQ ID NO:348)

**Toxin Sequence:**

20 Gly-Cys-Val-Xaa3-Ser-Gly-Xaa1-Ile-Cys-Xaa5-Phe-Met-Asp-His-Ile-Gly-Cys-Cys-Ser-Gly-  
 Lys-Cys-Thr-Phe-Val-Cys-Met-^ (SEQ ID NO:349)

-----

**Name:** Bu6.7  
**Species:** bullatus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

30 ATGAAACTGACGTGCGTGATGATCGTTACTGTGCTGTTCTTGACCGCCTGGACATTC  
 GTCACGGCTGATGACTCCACATATGGATTGAAGAATCTTTTGCCGAACGGACGTCAT  
 35 GAAATGATGAACCCCGAAGCCCCTAAATTGAACAAGAAAGATGAATGCTCTGCTCC  
 TGGTGCAATTTGTCTCATCAGGCCAGGACTCTGCTGCAGCGAGTTCTGCTTCTTTGCG  
 TGTTTTTAGTGACGGTTGATGTCTTCTACTCCCCTC (SEQ ID NO:350)

**Translation:**

10 MKLTCVMIVTVLFLTAWTFVTADDSTYGLKNLLPNGRHEMMNPEAPKLNKKDECSAP  
 GAFCLIRPGLCCSEFCFFACF (SEQ ID NO:351)

**Toxin Sequence:**

15 Asp-Xaa1-Cys-Ser-Ala-Xaa3-Gly-Ala-Phe-Cys-Leu-Ile-Arg-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-  
 Phe-Cys-Phe-Phe-Ala-Cys-Phe-^ (SEQ ID NO:352)

-----

**Name:** Bu6.8  
**Species:** bullatus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTACTGTGCTGTTCTTGACCGCCTGGACATTC  
 GTCACGGCTGATGACTCCAGAGACGCTCCGGATAGTGCAGAAGGATGGGAGAACT  
 TTTCTCGGAGGCACGTGACGAAATGAAGAACCGCAAAGACTTTGAATTGAGAGGGT  
 GCCTTCCTAGGTGGGAATTTTGTCCCATCTTTAAAAAAAACGATTGCTGCAGTGGCA  
 TATGCATAAGCATCTGCTTGTA AAACTCCGTGATGTCTTCTCTTCCCATC (SEQ ID  
 NO:353)

**Translation:**

MKLTTCVMIVTVLFLTAWTFVTADDSRDAPDSAEGWEKLFSEARDEMKNRKDFELRGC  
 LPRWEFCPIFKKNDCCSGICISICL (SEQ ID NO:354)

**Toxin Sequence:**

Gly-Cys-Leu-Xaa3-Arg-Xaa4-Xaa1-Phe-Cys-Xaa3-Ile-Phe-Lys-Lys-Asn-Asp-Cys-Cys-Ser-  
 Gly-Ile-Cys-Ile-Ser-Ile-Cys-Leu-^ (SEQ ID NO:355)

-----

**Name:** Sx6.4  
**Species:** striolatus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

ATGAAACTGACGTGCATGATGATTGTTGCTGTGCTGTTCTTGACCGCCTGGATATTT  
 GTAATGGCTGATGACTCCAGAAATGGATTGGAGAATCTTCCTCAGACTACACGTCA  
 CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACCAGACAGACTGCCTTGCTAAAG  
 ACGCTTTCTGTGCCTGGCCGATACTTGGACCACTGTGCTGCAGTCGCTTGTGCTTAT  
 ACGTCTGCATGtaaAACTGCCGTGATGTCTTCTACTCCCCTC (SEQ ID NO:356)

**Translation:**

MKLTMMIVAVLFLTAWIFVMADDSRNGI ENLPQTTRHEMKNPEASKLNQTDCLAKD  
 AFCAWPILGPLCCSRLCLYVCM (SEQ ID NO:357)

**Toxin Sequence:**

Asp-Cys-Leu-Ala-Lys-Asp-Ala-Phe-Cys-Ala-Xaa4-Xaa3-Ile-Leu-Gly-Xaa3-Leu-Cys-Cys-Ser-  
Arg-Leu-Cys-Leu-Xaa5-Val-Cys-Met-^ (SEQ ID NO:358)

5

-----

**Name:** Cn6.9  
**Species:** consors  
**Isolated:** No  
**Cloned:** Yes

10

**DNA Sequence:**

15

ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCACGGCTGATGACTCCAGAAATGGATTGGAGAATCTTTCTCCGAAGGCACGTCA  
CGAAATGAAGAACCCCGAAGCCTCTAAATCGAACAAGAGATATGAGTGCTATTCTA  
CTGGTACATTTTGTGGCATCAACGGAGGACTCTGCTGCAGCAACCTTTGCTTATTTT  
CGTGTGCTTAACATTTTCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:359)

20

**Translation:**

MKLTMMIVAVLFLTAWTFVTADDSRNGLENLSPKARHEMKNPEASKSNKRYECYST  
GTFCGINGGLCCSNLCLFFVCLTFS (SEQ ID NO:360)

25

**Toxin Sequence:**

Xaa5-Xaa1-Cys-Xaa5-Ser-Thr-Gly-Thr-Phe-Cys-Gly-Ile-Asn-Gly-Gly-Leu-Cys-Cys-Ser-Asn-  
Leu-Cys-Leu-Phe-Phe-Val-Cys-Leu-Thr-Phe-Ser-^ (SEQ ID NO:361)

30

-----

**Name:** Cn6.10  
**Species:** consors  
**Isolated:** No  
**Cloned:** Yes

35

**DNA Sequence:**

40

ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTTCTTGACCACCTGGACATTC  
GTCACGGCTGATGACTCCAGATATGGATTGAAGAATCTTTTCCGAAGGCACGTCA  
GAAATGAAGAACCCTGAAGCCTCTAAATTGAACAAGAGAGATGGGTGCTATAATGC  
TGGTACATTTTGTGGCATCCGTCCAGGACTCTGCTGCAGCGAGTTTGTCTTTTATGG  
TGCATAACATTTGTTGATTCTGGCTAACAGTGTGCGTTGGTTGATGTCTTCTACTCCC  
CTC (SEQ ID NO:362)

45

**Translation:**

MKLTCLMIVAVLFLTTFVTADDSRYGLKNLFPKARHEMKNPEASKLNKRDGCYNA  
GTFCGIRPGLCCSEFCFLWCITFVDSG (SEQ ID NO:363)

5 **Toxin Sequence:**

Asp-Gly-Cys-Xaa5-Asn-Ala-Gly-Thr-Phe-Cys-Gly-Ile-Arg-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-  
Phe-Cys-Phe-Leu-Xaa4-Cys-Ile-Thr-Phe-Val-Asp-Ser-# (SEQ ID NO:364)

10 -----

**Name:** Cr6.6  
**Species:** circumcised  
**Isolated:** No  
15 **Cloned:** Yes

**DNA Sequence:**

20 CGATCCATCTGTCCATCCATCTATTCATTCATTCGCTGCCAAACTGTATTAAATATTC  
AAGTCTCTCTTTCTGTTTGTGTCTAACAGATTGAGTAGGTGCATTCCTAGTGGTGATC  
TTTGTTCCTCCCTCGGATCACATAACAATGCTGCAATGCCAAGTGCGCATTCGTCTGCTT  
GTAAAACTGCCGTGATGTCTTCTCTCCCTC (SEQ ID NO:365)

**Translation:**

25 NRLSRCIPSGDLCFPSDHIQCCNAKCAFVCL (SEQ ID NO:366)

**Toxin Sequence:**

30 Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Asn-Ala-Lys-  
Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:367)

-----

35 **Name:** Cr6.5  
**Species:** circumcised  
**Isolated:** No  
**Cloned:** Yes

40 **DNA Sequence:**

CGATCCATCTGTCCATCCATCTATTCATTCATTCGCTGTCAAACCTGTATTAAATATTC  
AAGTCTCTCTTTCTGTTTGTGTCTAACAGATTGAGTTGGTGCATTCCTAGTGGTGATC  
TTTGTTCCTCCCTCGGATCACATAACAATGCTGCAGTGCCAAGTGCGCATTCGTCTGCTT  
45 GTAAAACTGCCGTGATGTCTTCTACTCCCTC (SEQ ID NO:368)

**Translation:**

NRLSWCIPSGDLCFPSDHIQCCSAKCAFVCL (SEQ ID NO:369)

**Toxin Sequence:**

Xaa4-Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Ser-Ala-Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:370)

**Name:** Cr6.5A  
**Species:** circumcicus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

CGATCCATCTGTCCATCCATCTATTCATTCATTCGCTGTCAAACGTATTAAATATTC  
AAGTCTCTCTTTCTGTTTGTGTCTAACAGATTGAGTAGGTGCATTCCTAGTGGTGATC  
TTTGTTCCTCCCTCGGATCACATAAATGCTGCAGTGCCAAGTGCGCATTCGTCTGCTT  
GTAAAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:371)

**Translation:**

NRLSRCIPSGDLCFPSDHIQCCSAKCAFVCL (SEQ ID NO:372)

**Toxin Sequence:**

Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Ser-Ala-Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:373)

**Name:** Cr6.6A  
**Species:** circumcicus  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

CGATCCATCTGTCCATCCATCTATTCATTCATTCGCTGCCAAACGTATTAAATATTC  
AAGTCTCTCTTTCTGTTTGTGTCTAACAGATTGAGTAGGTGCATTCCTAGTGGTGATC  
TTTGTTCCTCCCTCGGATCACATAAATGCTGCAATGCCGAGTGCGCATTCGTCTGCTT  
GTAAAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:374)

**Translation:**

NRLSRCIPSGDLCFPSDHIQCCNAECAVCL (SEQ ID NO:375)

**Toxin Sequence:**

- 5 Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Asn-Ala-Xaa1-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:376)

-----

- 10 **Name:** Cr6.5B  
**Species:** circumcised  
**Isolated:** No  
**Cloned:** Yes

15 **DNA Sequence:**

- CGATCCATCTGTCCATCCATCTATTCATTCATTCGCTGTCAAACGTATTAAATATTC  
 AAGTCTCTCTTTCTGTTTGTGTCTAACAGATTGAGTTGGTGCATTCCTAGTGGTGATC  
 TTTGTTTCCCCTCGGATCACATACGATGCTGCAGTGCCAAGTGCGCATTCGTCTGCTT  
 20 GTAAAACTGCCGTGATGTCTTCTTCCCATC (SEQ ID NO:377)

**Translation:**

NRLSWCIPSGDLCFPSDHIRCCSAKCAVCL (SEQ ID NO:378)

25

**Toxin Sequence:**

Xaa4-Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Arg-Cys-Cys-Ser-Ala-Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:379)

30

-----

- 35 **Name:** Cr6.6B  
**Species:** circumcised  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

- 10 CGATCCATCTGTCCATCCATCTATTCATTCATTCGCTGCCAAACGTATTAAATATTC  
 AAGTCTCTCTTTCTGTTTGTGTCTAACAGATTGAGTAGGTGCATTCCTAGTGGTGATC  
 TTTGTTTCCCCTCGGATCACATAAATGCTGCAATGCCAAGTGCGCATTCGCCTGCT  
 TGTAAACTGCCGTGATGTCTTCTTCCCCTC (SEQ ID NO:380)

15 **Translation:**

NRLSRCIPSGDLCFPSDHIQCCNAKCAACL (SEQ ID NO:381)

**Toxin Sequence:**

5 Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Asn-Ala-Lys-  
Cys-Ala-Phe-Ala-Cys-Leu-^ (SEQ ID NO:382)

-----

10 **Name:** Cr6.6C  
**Species:** circumcised  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

15 CGATCCATCTGTCCATCCATCTATTCATTCATTCGCTGCCAAACTGTATTAAATATTC  
AAGTCTCTCTTTCTGTTTGTGTCTAACAGATTGAGTTGGTGCATTCCTAGTGGTGATC  
TTTGTTCCTCCCTCGGATCACATACAATGCTGCAATGCCAAGTGCGCATTCGTCTGCTT  
GTAAACTGCCGTGATGTCTTCTACTCCCCCTC (SEQ ID NO:383)

**Translation:**

NRSLWCIPSGDLCFPSDHIQCCNAKCAFVCL (SEQ ID NO:384)

**Toxin Sequence:**

25 Xaa4-Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Asn-Ala-  
Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:385)

30 -----

35 **Name:** Cr6.7  
**Species:** circumcised  
**Isolated:** No  
**Cloned:** Yes

**DNA Sequence:**

10 CGATCCTCTGTCCTCCTCTATTATTATTCGCTGCCAACTGTATTAAATATTCAAGTCT  
CTCTTTCTGTTTGTGTCTAACAGATTGAGTTGGTGCATTCCTACTGGTGATCTTTGTT  
TCCCCTCGGATCACATACAATGCTGCAGTGGCAAGTGCACATTTCGTCTGCATGTAAA  
ACTGCCGTGATGTCTTCTCCTCCCCCTC (SEQ ID NO:386)

**Translation:**

15 NRSLWCIPTGDLCFPSDHIQCCSGKCTFVCM (SEQ ID NO:387)

**Toxin Sequence:**

Xaa4-Cys-Ile-Xaa3-Thr-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Ser-Gly-  
Lys-Cys-Thr-Phe-Val-Cys-Met-^ (SEQ ID NO:388)

5

-----

**Name:** Mn6.3  
**Species:** monachus  
**Isolated:** No  
**Cloned:** Yes

10

**DNA Sequence:**

15 ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCACGGCTGATGACTCCAGAAATGGATTGGAGAATCTTTCTCCGAAGGCACGTCA  
CGAAATGAAGAACCCCGAAGCCTCTAAATCGAACAAGAGATATGAGTGCTATTCTA  
CTGGTACATTTTGTGGCATCAACGGAGGACTCTGCTGCAGCAACCTTTGCTTATTTT  
CGTGTGCTTAACATTTTCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:389)

20

**Translation:**

MKLTMMIVAVLFLTAWTFVTADDSRNGLENLSPKARHEMKNPEASKSNKRYECYST  
GTFCCINGGLCCSNLCLFFVCLTFS (SEQ ID NO:390)

25

**Toxin Sequence:**

Xaa5-Xaa1-Cys-Xaa5-Ser-Thr-Gly-Thr-Phe-Cys-Gly-Ile-Asn-Gly-Gly-Leu-Cys-Cys-Ser-Asn-  
Leu-Cys-Leu-Phe-Phe-Val-Cys-Leu-Thr-Phe-Ser-^ (SEQ ID NO:391)

30

-----

**Name:** Sm6.5  
**Species:** stercusmuscarum  
**Isolated:** No  
**Cloned:** Yes

35

**DNA Sequence:**

10 ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC  
GTCACAGCTGATGACTCCATAAATGGACCGGAGAATAGACGAATATGGGAGAACT  
TTTGTTGAAGGCACGTGACGAAATGAAGAACCCCGAAGCCTCTCAATTGAGATGGT  
GCATTCCTAGTGGTGAACCTTTGTTTCCGCTCGGATCACATAAATGCTGCAGTGCCA  
AGTGCGCATTCGTCTGCTTGTAATACTACCGTGATGTCTTCTCCTCCCATC (SEQ ID  
15 NO:392)

**Translation:**



MKLTCMMIVAVLFLTAWTFVTADDSINGPENRRIWEKLLLKARDEMKNPEASQLRWCI  
PSGELCFRSDHIQCCSAKCAFVCL (SEQ ID NO:393)

5 **Toxin Sequence:**

Xaa4-Cys-Ile-Xaa3-Ser-Gly-Xaa1-Leu-Cys-Phe-Arg-Ser-Asp-His-Ile-Gln-Cys-Cys-Ser-Ala-  
Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:394)

10 -----

**Name:** Sm6.6  
**Species:** stercusmuscarum  
**Isolated:** No  
1.5 **Cloned:** Yes

**DNA Sequence:**

20 ATGAAACTGACGTGTGTGATGATCGTTGCTGTGCTGTTCTTGATCGCCTGGACATTC  
GTCACGGCTGATGACTCCAGAAATGGATTGAAGAATCTTTTCCGAAGGCACGTCAT  
GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGAGATGGGTGCTCTAGTGG  
TGGTACATTTTGTGGCATCCGTCCAGGACTCTGCTGCAGCGAGTTTGTCTTTCTTTGG  
TGCATAACATTTATTGATTGATGTCTTCTATTCCCCTC (SEQ ID NO:395)

2.5 **Translation:**

MKLTCVMIVAVLFLIAWTFVTADDSRNLKKNLFPKARHEMKNPEASKLNKRDCSSGG  
TFCGIRPGLCCSEFCFLWCITFID (SEQ ID NO:396)

30 **Toxin Sequence:**

Asp-Gly-Cys-Ser-Ser-Gly-Gly-Thr-Phe-Cys-Gly-Ile-Arg-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-  
Phe-Cys-Phe-Leu-Xaa4-Cys-Ile-Thr-Phe-Ile-Asp-^ (SEQ ID NO:397)

3.5 -----

**Name:** Sx6.5  
**Species:** striolatus  
**Isolated:** No  
10 **Cloned:** Yes

**DNA Sequence:**

1.5 ATGAAACTGACGTGCATAATGACCGTTGCTGTGCTGTTCTTGACCGCTTGGACATTC  
GTCACGGCTGATGACTCCAGAAATGCAATCGAGAATCTTCTTCTGAAGACACGTCA  
CGAAGTGGAAAACCCCAAAGCCTCTAGGTCGGGCGGTAGGTGCCGTCTTGGTGGTA  
CGGTTTGTGGCTTTCCGAAACCTGGACCATACTGCTGCAGTGGCTGGTGCTTTTTTGT

CTGCGCCTAAACCTGCCGTGATGTCTTCTCCTCCCATC (SEQ ID NO:398)

**Translation:**

- 5 MKLTCIMTVAVLFLTAWTFVTADDSRNGLENLLLKTRHEVENPKASRSGGRCRPGGTV  
CGFPKPGPYCCSGWCFFVCA (SEQ ID NO:399)

**Toxin Sequence:**

- 10 Cys-Arg-Xaa3-Gly-Gly-Thr-Val-Cys-Gly-Phe-Xaa3-Lys-Xaa3-Gly-Xaa3-Xaa5-Cys-Cys-Ser-  
Gly-Xaa4-Cys-Phe-Phe-Val-Cys-Ala-^ (SEQ ID NO:400)

-----  
15 **Name:** Sx6.6  
**Species:** striolatus  
**Isolated:** No  
**Cloned:** Yes

20 **DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACTGCCTGGACATTC  
GTCACGGCTGATGACTCCAAAAATGGACTGGAGAATCATTTTTGGAAGGCACGTGA  
CGAAATGAAGAACCGCGAAGCCTCTAAATTGGACAAAAAGGAAGCCTGCTATCCGC  
25 CTGGTACTTTTTGTGGCATAAAGCCCGGGCTATGCTGCAGTGAGTTGTGTTTACCGG  
CCGTCTGCGTCGGTGGTAACTGCCGTGATGTCTTCTATTCCCCTC (SEQ ID NO:401)

**Translation:**

- 30 MKLTCVMIVAVLFLTAWTFVTADDSKNGLENHFWKARDEMKNREASKLDKKEACYP  
PGTFCGIKPGLCCSELCLPAVCVGG (SEQ ID NO:402)

**Toxin Sequence:**

- 35 Xaa1-Ala-Cys-Xaa5-Xaa3-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-  
Xaa1-Leu-Cys-Leu-Xaa3-Ala-Val-Cys-Val-Gly-# (SEQ ID NO:403)

-----  
40 **Name:** Sx6.7  
**Species:** striolatus  
**Isolated:** No  
**Cloned:** Yes

45 **DNA Sequence:**

ATGAAACTGACGTGTCTGATGGCTGTTGCTGTGCTGTTCTTGACCGCCCGGACATTC

GTCACGGCTGATGACTCCAGAAATGGATTGGAGAATCTTTCTCCGAAGGCACGTCA  
CGAAATGAAGAACCCCGAAGCCTCTAAATCGAACAAGAGATATGAGTGCTATTCTA  
CTGGTACATTTTGTGGCATCAACGGAGGACTCTGCTGCAGCAACCTTTGCTTATTTT  
CGTGTGCTTAACATTTTCGTGATGTCTTCTATCCCCTC (SEQ ID NO:404)

5

**Translation:**

MKLTCLMAVAVLFLTARTFVTADDSRNGLENLSPKARHEMKNPEASKSNKRYECYST  
GTF CGINGGLCCSNLCLFFVCLTFS (SEQ ID NO:405)

10

**Toxin Sequence:**

Xaa5-Xaa1-Cys-Xaa5-Ser-Thr-Gly-Thr-Phe-Cys-Gly-Ile-Asn-Gly-Gly-Leu-Cys-Cys-Ser-Asn-  
Leu-Cys-Leu-Phe-Phe-Val-Cys-Leu-Thr-Phe-Ser-^ (SEQ ID NO:406)

15

-----  
**Name:** Sx6.8  
**Species:** striolatus  
**Isolated:** No  
**Cloned:** Yes

20

**DNA Sequence:**

25

ATGAAACTGACGTGTATGGTGATCGTCGCCGTGCTGCTCCTGACGACCTGTCATCTC  
ATCACAGCTGATGACTCCAGAGGTACGCAGAAGCATCGTTCCTGAGGTCGACTAC  
CAAAGTCTCCAAGTCGACTAGCTGCATGAAAGCCGGGTCTTATTGCGTCGCTACTAC  
GAGAATCTGCTGCGGTTATTGCGCTTATTTTCGGCAAAATATGTATTGGCTATCCCAA  
AAACTGATCCTCCCCCTACTGTGCTCTATCCTTTTCTGCCTGATGTCTTCTCCTCCCC  
TC (SEQ ID NO:407)

30

**Translation:**

MKLT CMVIVAVLLLTTCHLITADDSRGTQKHRSLRSTTKVSKSTSCMKAGSYCVATTRI  
CCGYCAYFGKICIGYPKN (SEQ ID NO:408)

35

**Toxin Sequence:**

Ser-Thr-Ser-Cys-Met-Lys-Ala-Gly-Ser-Xaa5-Cys-Val-Ala-Thr-Thr-Arg-Ile-Cys-Cys-Gly-Xaa5-  
Cys-Ala-Xaa5-Phe-Gly-Lys-Ile-Cys-Ile-Gly-Xaa5-Xaa3-Lys-Asn-^ (SEQ ID NO:409)

10

Xaa1 is Glu or  $\gamma$ -carboxy-Glu

Xaa2 is Gln or pyro-Glu

15 Xaa3 is Pro or hydroxy-Pro

Xaa4 is Trp or bromo-Trp

Xaa5 is Tyr, <sup>125</sup>I-Tyr, mono-iodo-Tyr, di-iodo-Tyr, O-sulpho-Tyr or O-phospho-Tyr

# is free carboxyl or amidated C-terminus, preferably amidated

## TABLE 2

### Alignment of Conotoxin Peptide Sequences

	8-GmVIA [F15Y]	-VKPCPKKEHQLCDPIFQN---CCF3WNC--VLF-CV^ (SEQ ID NO:4)
	8-GmVIA [F27Y]	-VKPCPKKEHQLCDPIFQN---CCF3WNC--VLY-CV^ (SEQ ID NO:5)
	8-maria9	M---CFHEAQLCDPIFQN---CCH3LFC--VLV-CV^ (SEQ ID NO:9)
10	Trk1.11	QVKPCPKKEHQLCDPIFQN---CCF3WYC--VVL3CT^ (SEQ ID NO:11)
	cm1.6	----CVPHF3PCNWLTDN---CC33YNC--IIFFCLE^ (SEQ ID NO:14)
	cm1.7	QVKPCPKKEHQLCDPIFQN---CCF3WYC--LLRFCL^ (SEQ ID NO:17)
	cm1.8	-VKPCSEEAQLCDPLSDN---CCF3WHC--VLV3CV^ (SEQ ID NO:12)
	8-TrkVIA [M8J]	W---CM3SEKCNLLDIN---CCL3Y-C--IVLVCT^ (SEQ ID NO:14)
15	cm1.4	----CLF3SEVCNIFFPN---CC33Y-C--ILLECT^ (SEQ ID NO:37)
	cm1.5	----CF3AESCEVISIN---CCQ3T-C--VFF-CL3^ (SEQ ID NO:40)
	cm1.6	----CF3AESCEVFSLE---CCT3L-C--LGF-CV3^ (SEQ ID NO:43)
	cm1.8	----CVF3F3PCNWLTDN---CC3EL-C--VFF-CL3^ (SEQ ID NO:16)
	cm1.5	----CF3AESCEVFSLE---CCT3I-C--LGF-CTW3^ (SEQ ID NO:43)
20	Trk1.2	----CL3AEVCNIFFPN---CC33Y-C--ILLFCA^ (SEQ ID NO:50)
	cm1.1	----CL3AEHETCNIFTN---CCF3V-C--IFI-CV3APE^ (SEQ ID NO:57)
	cm1.3	----CII3FDECIPIRHT---CCF3L-C--LLIACI^ (SEQ ID NO:60)
	cm1.4	----CL3F3EACIMLYCN---CC33Y-C--V3AICL^ (SEQ ID NO:63)
	Am1.1	----CH3NELCNIFIQN---CCH3T-C--LLI-CI3NP3^ (SEQ ID NO:66)
25	Am1.2	----CL3F3ELCNIFFPN---CC33Y-C--VLLVCL^ (SEQ ID NO:69)
	Am1.3	----CA33EELCIALD3N---CC33V-C--MVFFCL^ (SEQ ID NO:72)
	Am1.4	----CL3F3EACIMLYCN---CC33Y-C--V3AVCL^ (SEQ ID NO:75)
	Am1.5	----CVF3LDP3MLRHT---CCF3L-C--VLIACI^ (SEQ ID NO:78)
	Am1.6	----CL3F3ENCNIFFPN---CC33Y-C--VALVCL^ (SEQ ID NO:81)
30	Am1.4	----CII3FDP3MVRHT---CCF3L-C--VLIAC3TA^ (SEQ ID NO:84)
	Am1.7	----CK3E3EACNII3QN---CCL3K-C--DEF-CI3IPE^ (SEQ ID NO:87)
	8-maria3	----CII3F3ECNIFFPN---CC33W-C--IVLVCA^ (SEQ ID NO:90)
	8-maria1	----CL3F3E3CILFP3---CC33W-C--IVLVCA^ (SEQ ID NO:93)
	Marm1	----CL3F3EVCNIFFPN---CC33Y-C--VLLVCL^ (SEQ ID NO:96)
35	Marm1.2	----CQF3F3VCNIFFPN---CC33Y-C--VLLLCI^ (SEQ ID NO:99)
	maria7	----CII3FDP3CPIRHT---CCF3L-C--LLIACI^ (SEQ ID NO:102)
	maria1.1	----CL3F3EVCNIFFPN---CC33Y-C--VLLVCL^ (SEQ ID NO:105)
	6.8	SKKQCR3N3EVCNANL3N---CC33P-C--FLF-CLN3P^ (SEQ ID NO:108)
	Af1.3	----CT33SEL3VIDED---CC3NF-C--IIFFCLE^ (SEQ ID NO:111)
40	FF1A	----CA3F3ELCNIFFPN---CC33Y-C--VQFICL^ (SEQ ID NO:114)
	FFM1	----CL3AE3MCLL3NSK---CC33W-C--IILFCA^ (SEQ ID NO:117)
	FFM4	----CII3F3EIC3ILFP3---CC33W-C--IVLVCA^ (SEQ ID NO:120)
	FFM1	----CF3E3ELCNV3EIN---CC3TY-C--FIVVCH3^ (SEQ ID NO:123)
	FFM1	-IDEC3F33EFC3FFFI3P-PCC33W-C--FLW-CA^ (SEQ ID NO:126)
45	8. striatus S2	-IDEC3F33EFC3FFFI3P-PCC33W-C--FLW-CA^ (SEQ ID NO:129)
	cm1.5	-IDEC3F33EFC3FFFI3P-PCC33W-C--FFA-CA^ (SEQ ID NO:132)
	Am1.3	-IYDC3F33EFC3FFFI3P-PCC33W-C--FFA-CA^ (SEQ ID NO:135)
	Marr9	-IDDC3F33EFC3FFFI3P-PCC33W-C--FFA-CA^ (SEQ ID NO:138)
	cm1.4	-I---CL3F3NAFC3AWPIIGF-LCC33W-C--LYV-CM^ (SEQ ID NO:141)
50	cm1	-CDECI3ANK3NC3FFKLG3-PCC33CL-C--FFV-CA^ (SEQ ID NO:144)
	cm1.2	D--CII3F3F3CALPQL3L-LCC33F-C--LLF-CV^ (SEQ ID NO:147)
	Am1	-IG-C3NA3AFC3---IHFGLCC3FI-C--IVW-CT3^ (SEQ ID NO:150)
	8-PUVIA[F9A]	-FA-C3NA3STAC3---IKOGLCC3EF-C--LPGVC3G^ (SEQ ID NO:154)
	8-PUVIA[I12A]	-FA-C3NA3STFC3---AKOGLCC3EF-C--LPGVC3G^ (SEQ ID NO:155)
55	8-PUVIA[T8A]	-FA-C3NA3AFC3---IKOGLCC3EF-C--LPGVC3G^ (SEQ ID NO:156)
	cm1.1	-IG-C3NA3STFC3---IRPGLCC3EF-C--FLW-CITFVDC3^ (SEQ ID NO:159)
	cm1.2	-DE-CYPP3GTF3G---IKPGLCC3AI-C--LSFVC3IF-DE^ (SEQ ID NO:162)

M6.7  
 M6.3  
 E6.4  
 P6.4  
 5 8-SVIE [D1E]  
 8-SVIE  
 C6.1  
 C6.3  
 E6.2  
 10 F6.1  
 F6.3  
 G6.1  
 E6.1  
 E6.6  
 15 D6.3  
 A6.10  
 T6.10  
 G6.4  
 C6.1  
 D6.3  
 I6.7  
 E6.5  
 H6.6  
 H6.15  
 H6.10  
 25 H6.14  
 C6.1a14  
 C6.1  
 E6.4  
 30 E6.6  
 E6.7  
 E6.8  
 E6.5  
 E6.2  
 35 striat21  
 8Striatus 26  
 8Striatus 106  
 C6.3  
 E6.3  
 40 A6.1 (F763)  
 A6.11 (G21)  
 A6.12 (G20)  
 A6.5 (F08)  
 E6.5 (G211)  
 45 E6.1 (J425)  
 E6.2 (J424)  
 E6.3  
 E6.1 (G18)  
 E6.1 (F076)  
 50 E6.15 (A607)  
 E6.1 (F775)  
 M6.2 (G218)  
 M6.4 (A666)  
 E6.3 (F770)  
 55 Q6.1  
 Q6.2 (F034)  
 Q6.3 (F026)  
 T6.2 (F078)  
 T6.4 (F080)  
 60 T6.8  
 A6.1

-EA-CYNASSFCG---IH-ELCCSEF-C--ILW-CITFV13# (SEQ ID NO:165)  
 -EA-CYNASTFCG---IH-ELCCSAI-C--LSFVCISF-LF# (SEQ ID NO:168)  
 -EA-CYPBSTFCG---IH-ELCCSEL-C--LPAV/CVG# (SEQ ID NO:171)  
 -EA-CYPBSTFCG---IH-ELCCSEL-C--LPAV/CVG# (SEQ ID NO:174)  
 -E3-CINGSTFCG---IH-ELCCSEF-C--FLW-CITF11 (SEQ ID NO:177)  
 -D3-CNSSTFCG---IH-ELCCSEF-C--FLW-CITF11 (SEQ ID NO:180)  
 -Y3-C3NA3AFCS---IH-ELCCSEL-C--LVW-CT# (SEQ ID NO:184)  
 -Y3-C3NA3AFCS---IH-ELCCSEL-C--LGW-CT# (SEQ ID NO:187)  
 -YE-CYL1NHFCG---IH-ELCCSEL-C--LFFVCLTFS# (SEQ ID NO:190)  
 -E--CLF1YTICA---IH-ELCCSEL-C--MLV-CLF# (SEQ ID NO:193)  
 -II-CFPLVMFCG---VH-ELCCSEL-C--LLI-CV# (SEQ ID NO:196)  
 ---CYGSGTGCD---HNGCCSGW-C--IFA-CL# (SEQ ID NO:199)  
 ---CYGSGTGCD---HNGCCSGW-C--IFV-CL# (SEQ ID NO:202)  
 ---CFESWVACE---HNGCCSHV-C--LFV-CT# (SEQ ID NO:205)  
 ---CNEA3EHCT---HNGCCSES-CNKFVGECL# (SEQ ID NO:208)  
 ---CYGSGTSCN---HNGCCSW-C--IFA-CL# (SEQ ID NO:211)  
 ---CYGSGTSCN---HNGCCSW-C--IFVCL# (SEQ ID NO:214)  
 -I--CQALWYCPVPL3C-ICCY-ILIC--GPFVCISW# (SEQ ID NO:217)  
 KT--CQPFWDPCPGSLV-ITCCG-ILIC--FLFECV# (SEQ ID NO:220)  
 -I--CQPFWDYCPVPL3C-ICCY-ILIC--GPFVCISW# (SEQ ID NO:223)  
 -I--CQPFWDYCPVPL3C-ICCY-ILIC--GPFVCISW# (SEQ ID NO:226)  
 -G--CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:229)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:232)  
 -E--CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:235)  
 -I--CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:238)  
 -A--CSKFWYFCIFVIL-ICCY-ILIC--GPFVCISW# (SEQ ID NO:241)  
 -I--CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:244)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:247)  
 -I--CHNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:250)  
 -F--CTANSTFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:253)  
 -F--CTANSTFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:256)  
 -F--CTANSTFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:259)  
 -C--CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:262)  
 -D--CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:265)  
 -LWVCIP-ILIC--HNGCCS-IL-C--VF-CT# (SEQ ID NO:268)  
 ---WCIP-ILIC--HNGCCS-IL-C--VF-CT# (SEQ ID NO:271)  
 ---WCIP-ILIC--HNGCCS-IL-C--VF-CT# (SEQ ID NO:274)  
 -LWVCIP-ILIC--HNGCCS-IL-C--VF-CT# (SEQ ID NO:277)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:280)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:283)  
 -E--CVA3CHFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:286)  
 -D--CVA3CHFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:289)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:292)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:295)  
 -G--CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:298)  
 Q---CVA3CHFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:301)  
 -A--CVA3CHFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:304)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:307)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:310)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:313)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:316)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:319)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:322)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:325)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:328)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:331)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:334)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:337)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:340)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:343)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:346)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:349)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:352)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:355)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:358)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:361)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:364)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:367)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:370)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:373)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:376)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:379)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:382)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:385)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:388)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:391)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:394)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:397)  
 ---CLNVYFCGIFPVN-ELCCS-IL-C--VF-CT# (SEQ ID NO:400)

Ac6.2 -G--CVPSGEIC-YFMDHIG-CCSGK-CTF---VCM<sup>+</sup> (SEQ ID NO:349)  
 Bu6.7 -DE-CSAPGAFCL--IFPGL-CCSEF-C-FF--ACF<sup>+</sup> (SEQ ID NO:352)  
 Bu6.8 -G--CLPRWEFC-PIFFIND-CCSGI-CIS---ICL<sup>+</sup> (SEQ ID NO:355)  
 Cn6.10 -DG-CYNASTFCG--IFPGL-CCSEF-C-FL--WCITFVDS# (SEQ ID NO:364)  
 Cn6.4 -YE-CYSTGTFCG--INGGL-CCSNL-CLFF--VCLTFS<sup>+</sup> (SEQ ID NO:361)  
 Cr6.5 W---CIPSGILC-FPSDHIQ-CCSAK-CAF---VCL<sup>+</sup> (SEQ ID NO:370)  
 Cr6.5A ----CIPSGILC-FPSDHIQ-CCSAK-CAF---VCL<sup>+</sup> (SEQ ID NO:373)  
 Cr6.6 ----CIPSGILC-FPSDHIQ-CCNAK-CAF---VCL<sup>+</sup> (SEQ ID NO:387)  
 Cr6.6A ----CIPSGILC-FPSDHIQ-CCNAK-CAF---VCL<sup>+</sup> (SEQ ID NO:390)  
 Cr6.6B W---CIPSGILC-FPSDHIQ-CCSAK-CAF---VCL<sup>+</sup> (SEQ ID NO:399)  
 Cr6.6B ----CIPSGILC-FPSDHIQ-CCNAK-CAF---VCL<sup>+</sup> (SEQ ID NO:381)  
 Cr6.6C W---CIPSGILC-FPSDHIQ-CCNAK-CAF---VCL<sup>+</sup> (SEQ ID NO:289)  
 Cr6.7 W---CIPSGILC-FPSDHIQ-CCSGK-CTF---VCM<sup>+</sup> (SEQ ID NO:388)  
 Mn6.3 -YE-CYSTGTFCG--INGGL-CCSNL-CLFF--VCLTFS<sup>+</sup> (SEQ ID NO:391)  
 Sm6.5 W---CIPSGELC-FPSDHIQ-CCSAK-CAF---VCL<sup>+</sup> (SEQ ID NO:394)  
 Sm6.6 -DG-CSSG3TFCG--IFPGL-CCSEF-C-FL--WCITFID<sup>+</sup> (SEQ ID NO:397)  
 Sx6.4 -D--CLAKDAFCAPWPLGPL-CCSRL-CLY---VCM<sup>+</sup> (SEQ ID NO:398)  
 Sx6.5 ----CRFG3TVCGFPKI GPY-CC3GW-CFF---VCA<sup>+</sup> (SEQ ID NO:400)  
 Sx6.6 -EA-CYFPGTFCG--IFPGL-CCSEL-CLPA--VCV3# (SEQ ID NO:403)  
 Sx6.7 -YE-CYSTGTFCG--INGGL-CCSNL-CLFF--VCLTFS<sup>+</sup> (SEQ ID NO:406)  
 Sx6.3 STS-CMFASSYCVATTR--I-CC-3Y-CAYFGKICI3YPRN<sup>+</sup> (SEQ ID NO:409)

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It will be appreciated that the methods and compositions of the instant invention can be incorporated in the form of a variety of embodiments, only a few of which are disclosed herein. It will be apparent to the artisan that other embodiments exist and do not depart from the spirit of the invention. Thus, the described embodiments are illustrative and should not be construed as restrictive.

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